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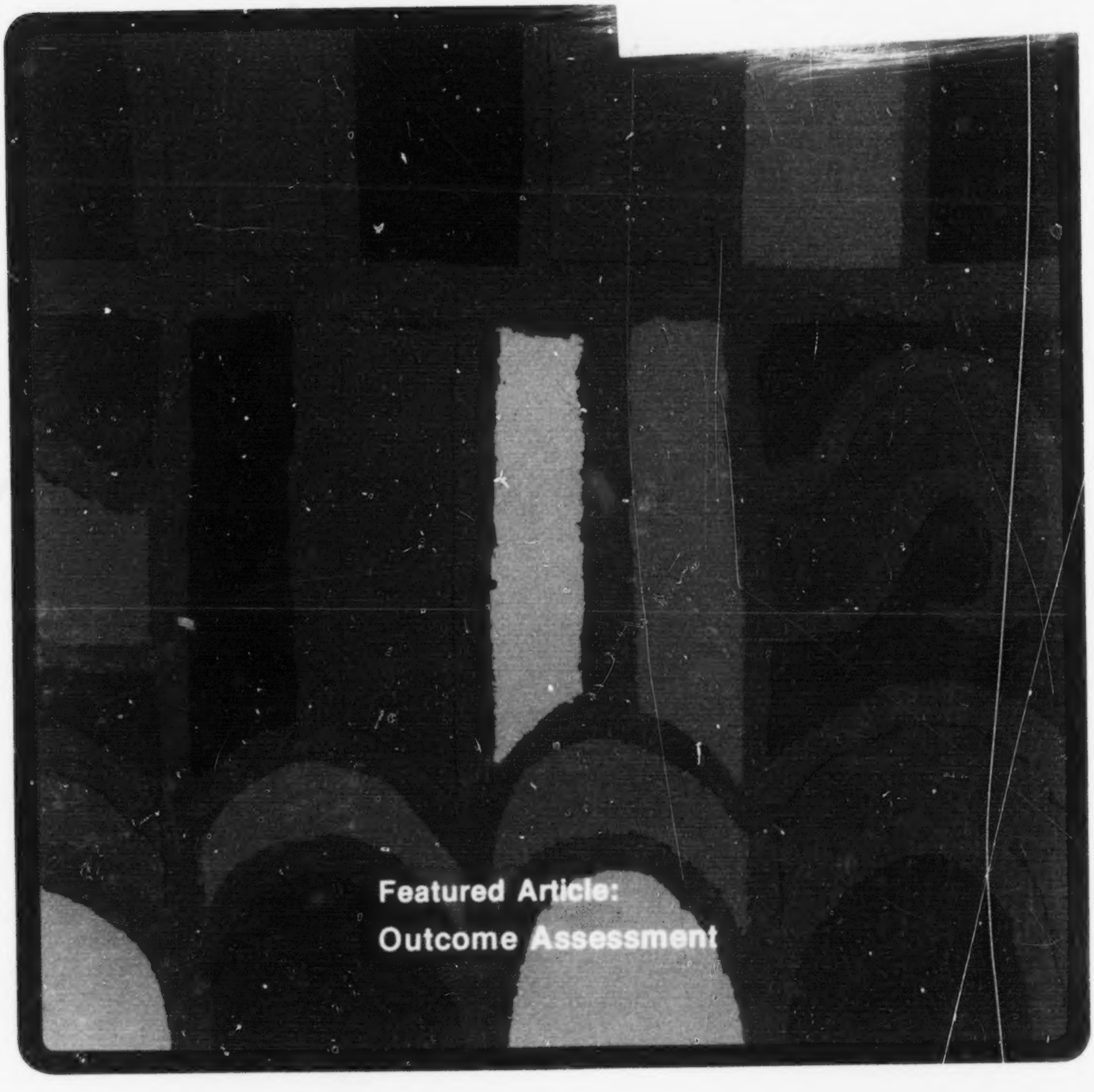

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Schizophrenia Bulletin National Institute of Mental Health

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About the Cover

The *Schizophrenia Bulletin* features art done by current and former mental hospital patients. The drawing that appears on the cover of this issue was sent to us by Julie Bry Schwab, Art Therapist, Mental Health Center of Boulder County, Boulder, Colorado. The artist, Gary Martinez, has provided the following description of his pastel drawing entitled, "A Famous Picture of an Unknown Artist":

The borders give a separateness to each color and enhance their contrast. The curved lines in relation to the sharp-angled lines create a border for my imagination. The colors of my imagination express my originality—something brilliant, something people have never seen before, something unusual, something different, something beautiful, and something imaginative. As opposed to anything that is commonplace and bland, the colors speak for me. I felt a feeling of gratification just knowing that I painted the picture (instead of my usual frustration before completion) and that the painting reflected my own style.

Feighner et al., Invisible Colleges, and the Matthew Effect

by Roger K. Blashfield

At Issue

In the article that begins below, Roger K. Blashfield traces the impact of a landmark article in American psychiatry—the publication by Feighner et al. in 1972 of a set of diagnostic criteria for use in psychiatric research. The author's focus is not on the scientific merits of the diagnostic criteria proposed by Feighner et al., but rather on the process by which these criteria came into widespread use in the psychiatric research community. Accompanying Dr. Blashfield's essay are commentaries by Samuel B. Guze, one of the originators of the Feighner criteria; Martin M. Katz and John S. Strauss, two scientists who have themselves made important contributions to the development of research diagnostic criteria; and R.E. Kendell, who offers—in addition to diagnostic expertise—an international perspective on this interesting phenomenon.

Comments from Schizophrenia Bulletin *readers are welcomed, and should be sent to At Issue, Center for Studies of Schizophrenia, Rm. 10-95, 5600 Fishers Lane, Rockville, MD 20857.* —The Editors.

Abstract

A citation analysis of an article published by Feighner et al. in 1972 has shown that it had a major impact on the literature about psychopathology. In fact, the Feighner article had over 70 times more citations than an average article published in the same journal. The Feighner article attracted attention partly because it had been created and promoted by the prolific St. Louis/Iowa group. The researchers associated with this group have advocated a neo-Kraepelinian approach to classification, and have had a powerful effect on classifications within American psychiatry during the 1970s. The influence of the neo-Kraepelinians provides an example of a process suggested by Deutsch (1966) concerning how changes in classificatory systems occur.

A journal article published by Feighner, Robins, Guze, Woodruff, Winokur, and Munoz (1972) in the *Archives of General Psychiatry* entitled "Diagnostic Criteria for Use in Psychiatric Research" is the focus of this article. It will emphasize the sociological aspects associated with the popularity of the Feighner et al. article, which proposed explicit diagnostic criteria to define 16 conventional classification categories. The 16 categories defined by Feighner et al. represented disorders such as schizophrenia, mania, depression, and anorexia nervosa, which these authors believed had been shown to be valid. The reason for using explicit criteria was to increase the reliability of the categories. In addition to the above, the Feighner article also mentioned five types of data which are necessary when validating categories in the classification of mental disorders.

As measured by citation frequency, the Feighner article has had a marked impact on the literature about psychopathology. From 1972 through 1980, there had been 1,157 citations to this article in the *Science Citation Index*. This was an average of 144.6 citations per year. In contrast, the average article published in the *Archives of General*

Reprint requests should be sent to Dr. R.K. Blashfield at Box J-256, J.H.M.H.C., Dept. of Psychiatry, Gainesville, FL 32610.

Psychiatry received only 2.1 citations per year. In other words, the Feighner et al. article had over 70 times the number of citations during an 8-year period as had an average article published in the *Archives of General Psychiatry*.

Why has this article attracted so many citations? Three possible answers are: First, the Feighner article was published in a prestigious journal. According to the Journal Ranking Package of the *Science Citations Index*, the *Archives of General Psychiatry* has the highest impact factor of all journals concerned with psychopathology (see table 1). Thus, the fact that the Feighner article was published in the *Archives* probably contributed to its impact. This factor alone, however, is insufficient to account for its popularity, as shown by the average number of citations per year to the Feighner article (about 145) compared to the average number expected for a typical article published in the *Archives* (about two).

A second possible factor is the reputation of the authors. All of the authors (Feighner, Guze, Munoz, Robins, Winokur, and Woodruff) were at Washington University in St. Louis at the time the article was written. One of the six, Winokur, became the chairperson at the University of Iowa in 1971, just before the article was published. The "St. Louis group," of which these authors were members, is a well-known collection of psychiatric researchers who have published a great deal on the topics of genetics, biochemistry, and classification of mental disorders. But since the Feighner article is the most frequently cited publication by members of the "St. Louis group," the prominence of the authors is again insufficient by itself to account completely for its popularity.

A third possible reason for the large number of citations is that it is a methodological article. Journal articles or books proposing a new methodology can attract a large number of citations. For instance, a book by Draper and Smith (1966) about linear regression has collected 2,760 citations in 15 years (about 184 citations per year). However, methodological articles and books concerning psychiatric classification generally have not had the impact which the Feighner article has demonstrated. For instance, Lorr (1966) edited a book in which cluster analysis methods were used to form new classifications of psychotic patients; Overall and Williams (1961) discussed different statistical models which could be used to help improve the diagnostic process; and Nathan (1967) published a book which contained a decision tree model to assign psychiatric diagnoses. Like the Feighner article, the intent of all three was to propose methodological alternatives to traditional clinical diagnosis that would improve the reliability of the diagnostic process. In total, the three works by Lorr, Nathan, and Overall and Williams have gathered only 102 citations—an average of 2.2 citations per year. Thus, the fact that the Feighner article suggested a new methodology concerning psychiatric classification does not sufficiently account for its high rate of citations.

In order to arrive at a better understanding of the impact of the Feighner article, an analysis was conducted on a randomly selected set of 50 journal articles that cited Feighner et al. The most striking feature about the 50 was that many were written by researchers at two different settings: Washington University in St. Louis, and the University of Iowa. In other words, 24 of the 50 articles were written by persons at the two universities that were the academic

Table 1. Relative frequency of citations (i.e., impact factor) for journals concerned with psychopathology

Journals	Impact factor
Archives of General Psychiatry	2.104
Biological Psychiatry	1.626
American Journal of Psychiatry	1.482
British Journal of Psychiatry	1.172
Journal of Abnormal Psychology	1.124
Journal of Nervous and Mental Disease	.921
Journal of Psychiatric Research	.857
Diseases of the Nervous System	.752
Acta Psychiatrica Scandinavica	.639
Comprehensive Psychiatry	.430
Journal of Clinical Psychology	.367

Note: These data are from the "Journal Ranking Package" of *Science Citations Index* (1976, Volume 9). Impact factor is defined as the total number of 1974 citations to articles published in the target journals during 1972–73 divided by the total number of source articles per target journal in 1972–73.

homes of the authors of the Feighner article. Of the remaining 26 articles, nine articles had authors who had been psychiatric residents at Washington University. Thus 60 percent of the 50 randomly chosen articles citing Feighner et al. were written by authors who at some time had been at St. Louis or Iowa.

This clustering of authors can also be documented through an analysis of citation frequency by author. From 1972 to 1974, 18 authors cited Feighner et al. more than once. Of these 18 persons, only two (Robert Spitzer and J.J. Schildkraut) had not been directly associated with either Washington University or the University of Iowa. Of the 58 authors who cited the Feighner article more than once from 1975 to 1977, 21 had been at Washington University or Iowa. This suggests that most of the early citations to the Feighner article were by members of the St. Louis/Iowa group while, more recently, the article has attracted attention among other groups of researchers.

Invisible Colleges and the Matthew Effect

The analysis of citations to the 1972 journal article by Feighner et al. demonstrates two major concepts which have been discussed within the literature on the sociology of science: (1) invisible colleges and (2) the Matthew effect. The concept of *invisible college* was first used in the 17th century to refer to the collection of scientists who eventually formed the Royal Society of London (Cole and Zuckerman 1975). The noun "college" was used to describe such a group of scientists because, like the faculty of a college, the group represented a collection of intellectuals who had a sense of allegiance to each other and who frequently interacted both professionally and socially. The adjective "invisible" was used because the membership of the group was not confined to a particular academic setting, and was not obvious to persons who had little knowledge about 17th century science. In 1963, Price reintroduced the term "invisible college" to describe the existence of such groups in modern sciences. These groups are collections of scientists who live in disparate geographical locations, but who often attend the same conferences, who publish in the same journals, who invite each other to give presentations at their home institutions, and who share preprints of their research endeavors. It is through the political power of such "colleges" that many of the changes in a science are made.

An important point to note about the concept of invisible colleges is that it is not intended to connote a conspiratorial or subversive process in which power groups engage in Machiavellian struggles for control of a science. As the concept has come to be used by sociologists, the existence of invisible colleges occurs in every science and virtually every researcher/scientist can be identified as belonging to some particular invisible college (Crane 1972). In fact, when Price (1963) first introduced the term, he was using it to describe how scientists must form into reasonably small, homogeneous groups in order to protect themselves from the pressures of "Big Science," the "publish or perish" ethic, and the tremendous explosion of scientific literature. All of these forces are sufficiently powerful to overwhelm virtually any scientist who attempts to remain isolated and yet make significant advances in his or her field. It is through the formation of small, informal collegial groups that individual scientists can gain sufficient support and power to become effective.

The citation analysis of Feighner et al. demonstrates the existence of an invisible college within modern psychiatric classification. A large percentage of citations to the Feighner article have been made by researchers who are or had been at the University of Iowa or Washington University, suggesting that there exists an invisible college associated with the St. Louis/Iowa group approach to descriptive psychiatry. Gradually this "college" has expanded to include psychiatrists at New York State Psychiatric Institute, UCLA, UCSD, Southern Illinois University, and the University of Kentucky.

The presence of this invisible college has also been discussed in an article by Klerman (1978). He associated this college with the biological psychiatry movement, which was formed during the 1960s and became a powerful force in American psychiatry during the 1970s. Klerman had given the members of this "college" the name "the neo-Kraepelinians." According to him, the most prominent members of the neo-Kraepelinian movement were Robins, Guze, Winokur, Klein, and Spitzer. The first three individuals are all co-authors of the Feighner article while the last two are currently at the New York State Psychiatric Institute, which is described above as an associated setting for this invisible college.

Klerman used the name "neo-Kraepelinian" to describe this invisible college because the principles of classification assumed by these researchers were similar to the principles inherent in Kraepelin's approach to classification (Kahn 1959). That is, these psychiatrists all strongly advocated a scientific approach to classification, supported the medical model, engaged in biological research, and eschewed the psychoanalytic perspective which had dominated psychiatric thinking in the United States. Table 2 lists nine propositions which collectively form the basic beliefs of the neo-Kraepelinian invisible college.

Table 2. Neo-Kraepelinian credo

1. Psychiatry is a branch of medicine.
2. Psychiatry should utilize modern scientific methodologies and base its practice on scientific knowledge.
3. Psychiatry treats people who are sick and who require treatment for mental illness.
4. There is a boundary between the normal and the sick.
5. There are discrete mental illnesses. Mental illnesses are not myths. There is not one but many mental illnesses. It is the task of scientific psychiatry, as of other medical specialties, to investigate the causes, diagnosis, and treatment of these mental illnesses.
6. The focus of psychiatric physicians should be particularly on the biological aspects of mental illness.
7. There should be an explicit and intentional concern with diagnosis and classification.
8. Diagnostic criteria should be codified, and a legitimate and valued area of research should be to validate such criteria by various techniques. Further, departments of psychiatry in medical schools should teach these criteria and not depreciate them, as has been the case for many years.
9. In research efforts directed at improving the reliability and validity of diagnosis and classification, statistical techniques should be utilized.

Reprinted with permission from Klerman, G.L. The evolution of a scientific nosology. In: Shershow, J.C., ed. *Schizophrenia: Science and Practice*. Copyright © Harvard University Press, 1978.

Neo-Kraepelinians had a major impact on psychiatric thinking about classification during the 1960s. First, it was the members of this college who wrote and promoted the Feighner article. In the mid-1970s Spitzer, Endicott, and Robins (1975) created the *Research Diagnostic Criteria* (RDC). The RDC proposed explicit diagnostic criteria for the schizophrenic and affective disorders and were incorporated in much of the research on these disorders being sponsored by NIMH during the late 1970s. In addition, the RDC was a precursor to the new *Diagnostic and Statistical Manual of Mental Disorders*, i.e., the *DSM-III* (American Psychiatric Association 1980). Ten of the 19 members of the psychiatric task force which created the *DSM–III* were members of the neo-Kraepelinian college. After a number of revisions, critical comments by researchers, and a set of field trials, the *DSM–III* became the official classification of American psychiatry in 1980.

The second important concept from the sociology of science which can be used to understand the dramatic number of citations to the Feighner article is the *Matthew effect*. The effect was first described by Merton (1968). This effect is named for a verse in the Gospel according to Matthew which says "For unto every one that hath shall be given, and he shall have abundance; but from him that hath not shall be taken away even that which he hath" (Matthew 25:29). The Matthew effect refers to the fact that most persons who publish journal articles receive very few citations to their articles (they hath not). On the other hand, there are a smaller number of persons who also publish articles in scientific journals, and their articles frequently attract a large number of citations (they hath abundance). The latter researchers have established reputations, are likely to serve on editorial boards in their areas, are more likely to receive research grants, etc.

After its initial promotion by members of the neo-Kraepelinian movement, the number of citations to the Feighner article showed a rapid growth. A likely contributing reason for this rapid growth of citations is the Matthew effect. The Feighner article had four prolific co-authors (Guze, Robins, Winokur, and Woodruff) whose publications had already been demonstrated to "hath abundance." In addition, the relatively large number of early citations to this article (i.e., almost 100 citations before 1975) increased the probability that the article would attract the attention of other researchers. In short, the initial promotion of the Feighner article by the St. Louis/Iowa invisible college was compounded by the Matthew effect into generating an enormous number of citations.

Discussion

Historians and sociologists who have studied the process of science have suggested that two types of forces can be used to account for changes within any science. The first force is the *cognitive* (internal, scientific) force which concerns the quality and amount of evidence supporting any innovation in a science before it is adopted. It is the cognitive aspect which researchers are trained to emphasize. Theories, hypotheses, methodologies, statistics—these are the cognitive aspects of science which supposedly determine if a piece of research is to be accepted. The second force involved in scientific change is the *noncognitive* (external, extrascientific) which pertains to religious beliefs, metaphysical conceptions, socioeconomic issues, and internal politics.

The entire focus here has been on the "noncognitive" aspects of the Feighner et al. article. No discussion has been directed at the scientific merit of the diagnostic criteria proposed by the St. Louis group. Journal articles by Helzer et al. (1977); Brockington, Kendell, and Leff (1978); Overall and Hollister (1979); and Fenton, Mosher, and Matthews (1981) address the issue of scientific merit of the Feighner criteria, especially when these criteria are used to define schizophrenia.

Although this article has focused on noncognitive forces, it was not meant to imply that scientific merit was unrelated to the wide impact of the Feighner et al. article. Historians of science generally agree that the alterations in a science rarely result from either cognitive or noncognitive factors alone (MacLeod 1977). The reason for examining noncognitive factors here is the fact that these factors, as they influence the classification of mental disorders, have been largely ignored.

Concerning the noncognitive aspects of change within a classification, the Feighner et al. article provides a dramatic example of an argument proposed by Deutsch (1966). He suggested that most changes in the language system of a science will be effected by a small group of scientists of related interest forming a collective body. As the group solidifies its ideas, it will create its own jargon of new classificatory concepts or new definitions of old concepts. It follows that as the power and prestige of this group increases within its scientific domain, its jargon will gain acceptance.

The process of change described by Deutsch appears to describe the growth of influence by the neo-Kraepelinians. The psychiatrists who favored the biological approach to psychiatry and who believed in the medical model formed an "invisible college." Many of these psychiatrists were at or had been associated with Washington University in St. Louis or the University of Iowa (or, later, with the New York State Psychiatric Institute). Because of their emphasis on science and research, this group became concerned with classification and proposed a set of diagnostic criteria which could be used in research. As the influence of the neo-Kraepelinians spread, their diagnostic criteria gathered a great deal of attention, were frequently cited, and finally became the basis for diagnostic definitions used in the new psychiatric classification, the *DSM-III*.

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The Author

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Comments on Blashfield's Article

Since Roger Blashfield was candid enough to reveal that he had unsuccessfully submitted this manuscript to five other journals before it was accepted by *Schizophrenia Bulletin*, I want to note, at the beginning, that I had been asked to review the manuscript three times, including the last time by *Schizophrenia Bulletin*, and that I had recommended acceptance each time. I think I did so for several reasons. He had made an interesting observation (there are never too many of these); it was flattering and reassuring to see documented our own impression about the impact of our article and our work; and it might reinforce such impact by making it explicit and objective.

At the same time, I had a vague sense of uneasiness: Would Blashfield's article lead to some backlash from the field? Would it stimulate an organized effort against the importance of diagnosis in psychiatry on the part of many who have never accepted the premises underlying the medical model for psychiatric disorders? Would this backlash focus on the sociological aspects of the phenomenon (what Blashfield refers to as noncognitive features) as a means of trying to undercut the validity of what we have been trying to do instead of dealing with the scientific or "cognitive" aspects? Despite these misgivings, I voted for publication, partly in obedience to my sense of intellectual integrity and partly out of curiosity to see what the field would make of his article.

As a sociological observation, his article is tantalizing and somewhat frustrating, because it is ahistorical and because it ignores the broad sociological context of the field at the time our article was written and published. Blashfield has nothing to say about the state of American psychiatry during the 1950s, 1960s, and early 1970s. By not tracing the drift of American psychiatry away from its medical base during the 25 years before our article's publication, and by not relating our ideas to those in ascendancy at the time, he runs the risk of creating the impression, though he warns against it, that our article arose out of some secret cabal or conspiracy designed to establish our ascendancy.

A sociological analysis may be interesting and legitimate, but it should certainly try to consider major relevant sociological forces if it is to achieve validity. A sociological study of an idea or viewpoint, to be most effective, should relate the idea or viewpoint to others that are connected historically and contemporaneously. Otherwise, a "noncognitive" analysis will, in the final analysis, be no more than a footnote.

Perhaps of greater moment is Blashfield's decision not to deal with the "*cognitive* (internal, scientific) force" of our article. After reviewing the evidence, he concluded that the impact of the article was not explained by the status of the journal in which it appeared, by the reputation of its authors, or by the fact that it was a methodologic article. These were the only hypotheses he tested. He nowhere suggests that the impact of the article may have resulted from the fact that it met an important scientific need at a time when American psychiatry was slowly and imperfectly groping its way back to medicine. By deliberately choosing not to deal with any question of scientific substance, Blashfield appears to build a major edifice on a single, ultimately flimsy support.

The scientific question—and finally the sociological question—was and is: Can we have a scientific psychiatry without a serious, systematic effort to develop a valid classification of psychopathology? Our answer was and is: No! We proposed a new beginning for the scientific endeavor. We believe that the impact of our article was directly related to the validity of our premise—not to the formation of an "invisible college." To the extent there was such a "college," it facilitated the spread of the value of our premise, but here, as elsewhere, it is important to distinguish between the message and the messenger.

We believe that scientific progress in psychiatry (as in the rest of medicine) comprises two broad streams of investigation. One attempts to account for clinical manifestations over time as functions of geographic, climatic, nutritional, social, economic, familial, and therapeutic factors; the other attempts to account for them in terms of cellular and molecular bodily processes (in this case of the brain). The two approaches, one epidemiological and the other neurobiological, are inherently complementary. Each *requires*, *reinforces*, and ultimately *validates* a classification of psychopathology. Classification is indispensable for thinking, studying, teaching, and communicating. Our article was based on this fundamental premise. Classifications begin somewhere, but they are constantly changing and becoming more sophisticated as scientific fields mature. Our article was a proposal for a new beginning in a discipline that for a generation had rejected our premise. The impact of our article, in my opinion, reflects only that psychiatry wants to reidentify with its medical base, by committing itself anew to that quintessential medical activity: diagnosing illness. Physicians have always recognized that diagnosis is not enough, but they have also intuitively and explicitly recognized that diagnosis is the keystone of medical practice and clinical research. We proposed that the situation is not different in psychiatry, and many colleagues now agree.

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Describing the history of diagnostic systems, Menninger (1963) coined the phrase "the epidemiology of taxonomy" to suggest the processes by which new concepts spread. In this report, Blashfield effectively describes a current manifestation of these processes. Such an attempt to understand factors that determine the development and extension of concepts in psychiatry is extremely important for the perspective it provides on the way we carry out practice and research. Analogous issues are involved in considering support or attack of the "medical model," and other key concepts.

A major issue raised by Blashfield's report is very similar to a question repeatedly discussed in the field of history: Is it the person, or in this instance, the persons, who generate a situation, or is it the times more generally? Tracing the recent shifts in American diagnostic practice, Blashfield makes an impressive argument for the role of persons involved, their positions, and their productivity. These seem important in providing considerable impetus for the acceptance of our current descriptive diagnostic concepts.

But such concepts exist in a temporal context, and it is equally important in understanding their development to consider this context. If, as has been suggested, science develops in cycles and is mediated to some extent by geographic or academic "schools," then one can see any shift (or paradigm shift) as reflecting a segment of such a cycle. Thus, Louis' 19th century contribution in promoting a descriptive approach to tuberculosis contrasted with the previous orientation toward speculative theorizing, and Claude Bernard's similar approach to general medicine around the same time had a comparable role. Both efforts appear to reflect recurring shifts similar to the recurring shifts in the opposite direction. Such opposite shifts are reflected by the periodic flowering of theoretical structures focusing on underlying processes (e.g., those by Koehler, Piaget, Freud) in order to progress beyond "blind empiricism."

A problem with such theoretical structures has been the tendency to expand them far beyond their empirical base, and then, sometimes using concepts that cannot be tested, to dominate practice, research, education, financial resources, and prestige. But the same can be said for more purely descriptive approaches. These have been accused of being sterile, rarely progressing beyond counting and describing, and coming to dominate their era far beyond what is empirically justified. Of course, even descriptive approaches are more theoretical than is often claimed, since crucial assumptions are involved—often implicitly—about the nature of acceptable data (e.g., excluding vague feelings) and how the collecting and clustering of data should take place. If, for example, one reads Lara Jefferson's (1964) description of what it is like to be insane, and then Kraepelin's textbook accounts of psychoses, it appears that Kraepelin almost totally ignores the characteristics of psychotic disorder as someone like Lara Jefferson experiences them.

When the cycles between descriptive and theoretical emphasis are recognized, a particularly important contribution of Blashfield's report is that it suggests one way in which the pendulum swing begins and then develops the potential for becoming extreme. This extreme swing tends to disqualify first the preceding orientation and then, ironically, to disqualify itself as it becomes accepted as the complete solution and is ultimately challenged. Although such swings from one extreme to the other may or may not reflect an optimal way for science to progress, one of their serious disadvantages is that they inhibit the synthesis of the orientations involved. If, as seems most likely to me, both descriptive and theoretical, process-oriented approaches are essential but incomplete in themselves, the swinging pendulum makes especially difficult any attempts at synthesis that might best reflect the entire condition to be studied.

Blashfield's article makes a useful point, but a more complete picture of the situation in my opinion needs also to include the hunger that the field has had to proceed beyond the vagueness and pseudo-communication that marked psychiatric diagnosis in the 1950s and 1960s, a vagueness especially severe in the United States. Such limitations in diagnostic concepts and reliability severely impeded systematic research, or even learning. Although American psychiatry during that period made major contributions in psychological, developmental, and humanistic approaches for even the most severe types of psychopathology (led by Meyer, Sullivan, Fromm-Reichmann, Menninger, and many others), often we had seriously distanced ourselves from a more testable empirical base. Thus, what Blashfield calls a neo-Kraepelinian tradition appears to reflect the pendulum swing away from an extreme in the opposite direction. In fact we may now have gone even further than Kraepelin, who employed such concepts as the "will," which we have shunned, apparently because of their imprecision.

The question, it seems to me, is can we have both? Can we maintain an active respect and investment in descriptive criteria and reliable data, while including an equal respect for the subjective experiences of psychiatric disorder, for theory and postulated underlying processes? Failure to use both orientations is perhaps the most unscientific approach of all. Ignoring the range of data that appears to be relevant to our field or denying that we have conceptual structures which select and organize our perception, learning, and teaching seems a most inadequate reflection of reality. "Colleges" do seem to exist and to have an important effect, but they exist within a context, and to deal with this context, we must recognize its vicissitudes over time.

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It is always useful to have the attention of the field called to the less obvious forces which generate a particular direction in science. As Blashfield points out, there may be strong *scientific* bases for the influence of the article by Feighner et al., but there are, also, other sociologic forces at work which serve to increase its popularity and its palatability to the field at large. The article did not, after all, present a major scientific discovery, a "breakthrough"; it did not even report a new innovative method which could be expected to open the doors of discovery. The Feighner criteria are, in the simplest of terms, a set of definitions of already accepted concepts which are "operational" in nature, and which permit common language and common criteria to be applied in the description and classification of patients and their disorders. As Blashfield points out, such systems had already been developed by others—systems which appeared to be further along in their development and whose reliability had already been tested; yet, these systems received little attention or application. The Feighner system has benefited from the fact that it came out of a traditional and increasingly resurgent school of psychiatry, the neo-Kraepelinian, that it was backed by a respected, highly influential university department of psychiatry, and that it was published in the most prestigious of psychiatric research journals.

There are other reasons, scientific and sociologic, which Blashfield overlooks, which may underlie differences in the influence of various research efforts in the field of classification, and they are worth noting:

- The Feighner criteria came along at just the right time. Psychobiologic research, which had had new life breathed into it by the introduction of the major tranquilizers in the 1950s, was in serious need of objective, scientific classification systems for the mental disorders. The standards in this field were increasingly being raised by the influence of the new scientific community in psychiatry, by the National Institute of Mental Health (NIMH), and by the psychiatric research journals, particularly the *Archives of General Psychiatry* and the *Journal of Psychiatric Research.*

- NIMH placed increased emphasis in the early 1960s on the need to improve methodology generally, in the field of clinical research, but particularly in its program in psychopharmacology (Cole and Gerard 1959). This meant improved methods for the "primary prerequisites" (Kety 1968) in the development of a science, i.e., description and classification, and, secondly, for the evaluation of changes in psychopathology. This increased attention began with an early influential conference on psychopharmacology (Cole and Gerard 1959) and continued for the field of clinical research generally (Katz, Cole, and Barton 1968), and later specifically for the affective disorders (Williams, Katz, and Shield 1972).

The field of psychiatric research is actually much smaller than it appears. Most of the sound work in progress is supported through research grants from the NIMH. The scientific groups and the Institute staff that monitor the award of these grants require that the methodology in these areas be sound. Investigators have had to strengthen these basic aspects of their program, i.e., classification, to qualify for grant support.

- Finally, as regards the NIMH role, a group of investigators under its auspices, and as part of a collaborative program on the Psychobiology of the Depressive Disorders (Katz et al. 1979), "commissioned" a team in 1972, R. Spitzer, E. Robins (Washington University), J. Endicott, and J. Mendels, to refine the Feighner criteria, to produce a revised set of research diagnostic criteria (RDC), and to create standardized methods for its application in psychobiological research. That has since been done, and in tandem with the more recently developed Schedule for Affective Disorders and Schizophrenia (Endicott and Spitzer 1978), the RDC has had a major impact on the development of the *DSM-III* (American Psychiatric Association 1980). Thus, the NIMH was directly instrumental in increasing the awareness of the scientific and clinical community of the importance of this specific development for advancing research in psychiatry.

There is no question, therefore, that several forces were at work in increasing the visibility of the Feighner et al. article. Most of these influences we have to consider as healthy for the development of science in this area. Nevertheless, to return to Blashfield's major point, why were other bodies of research apparently as sound technically and with the basic psychometric work already accomplished (e.g., Lorr's and Overall's systems) relatively ignored by psychiatry?

Part of the reason, I believe, reflects disciplinary insulation. Lorr and Overall are psychologists, and they tend to publish in journals that are not easily accessible to psychiatrists. Psychologists are also less influenced generally by what appears in psychiatric journals. By the same token, clinical psychiatrists tend to be uncomfortable with the kind of quantitative approaches developed by psychologists for what they [illegible] as essentially "judgmental" problems. They tend to believe that diagnosis is a "psychiatric" not a "psychological" problem, and that psychiatrists are in a better position, through experience and perspective, to solve it. This, again, is one of those social rather than scientific issues to which Blashfield alludes.

Finally, it is worth commenting on the most complex of the issues surrounding classification: the potentially conflicting purposes and interests of scientists and clinicians in developing such systems. It is too often assumed that the purposes for which classification systems are developed are the same for clinicians, for scientists in psychopathology, and for epidemiologists. Morton Kramer, the former head of Biometrics at NIMH, has been eloquent on the confusion created by this assumption, and one has only to review the separate perspectives of the various disciplines as presented in a section of the *Role and Methodology in Classification in Psychiatry and Psychopathology* (Katz, Cole, and Barton 1968) to appreciate the size and significance of the gaps in their conceptualization of the issues of classification and diagnosis. The clinicians, for example, need a system which will communicate easily, and which will assist in predicting the results of treatment. Scientists see classification as an ultimate objective in which the "natural" order is represented and, in the case of psychopathology, as based primarily on etiology. These different objectives result in different values as to which studies and which evidence are worth considering. All these perspectives are obviously important.

Despite these conflicting elements, there have been major developments in this field over the past 25 years; new evidence and new systems have been produced in research from several of the disciplines. Perhaps it is time again to go beyond the assembling of committees to discuss the relative values of *DSM-III* and *ICD-9*, Feighner and the RDC, the Present State Examination (Wing, Cooper, and Sartorius 1974) and the SADS, and to examine the accumulating evidence on the nature of the depressive disorders and of schizophrenia, psychological and biological, with a view toward developing more objectively grounded empirical systems of classification.

We should be somewhat beyond the development of the RDC phase, the "operational definitions" in this field, and be able to review new evidence in the service of creating the most effective systems for these various objectives.

It may be time to rise above the social issues, to reexamine the problem in a more scholarly context, possibly a new NIMH sponsored conference on "the state of research on classification in psychopathology."

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Roger Blashfield's concern is focused on the frequent citation of the 1972 paper by Feighner, Robins, Guze et al., which he sees partly as cause and partly as effect of the rise to power of a "neo-Kraepelinian" school of psychiatry based on a St. Louis-New York axis. His stance seems to me to fall uneasily between that of disinterested commentator and unsuccessful competitor. The former tries to offer a detached commentary on the social process by which a group of like-minded scientists achieves a position of dominance, but the latter cannot quite conceal his resentment at being on the losing end of the "Matthew effect" he describes.

From an imperfect vantage point on the far side of the Atlantic, it seems to me that, although Blashfield's factual account is quite accurate so far as it goes, his analysis of why the influence of the St. Louis school increased so dramatically in the 1970s is inadequate and incomplete. Eli Robins and his colleagues in St. Louis had been energetically pursuing essentially the same type of research for many years before 1972, and had been almost totally ignored, at least in North America. Nor were they themselves responsible for the revolution that brought them to power. As Thomas Kuhn has emphasized, scientific revolutions are always preceded by a crisis; an established paradigm is only replaced by a new one because it is manifestly failing in some crucial respect. Psychiatry's crisis was caused by the repeated demonstration that the reliability of psychiatric diagnoses was horrifyingly low, that key terms like schizophrenia were being used imprecisely and indiscriminately, and that in consequence fruitful research was seriously handicapped. The need for operational definitions of diagnostic terms had been pointed out by Carl Hempel as long ago as 1961. Members of the St. Louis school were the first to put his advice into practice, partly because it could readily be incorporated into their existing research tradition, and partly because they had the energy to do what other people like myself were merely advocating. Things rapidly gathered momentum from that time on for a variety of reasons, of which a convergence of interests between Spitzer's group in New York and Eli Robins' proteges was only one. Klerman at ADAMHA must have had a considerable influence on the direction and scale of government research funding in the 1970s, and his lineage was Yale and Harvard rather than St. Louis or New York. Other workers like Mendels in Philadelphia and Abrams and Taylor at Stonybrook were also part of the movement despite having no prior allegiance to either Washington University or the New York State Psychiatric Institute. In this context there is nothing very surprising about the large number of citations the Feighner article obtained. As Blashfield himself says, methodological articles tend to be cited more frequently than those concerned with research findings if they describe an important technical innovation, and I imagine the Rorschach test, the MMPI, the

Hamilton Rating Scale, and the EPI all still show a healthy lead over Feighner's article.

The "invisible college" phenomenon Blashfield describes is, as he says, characteristic of the way scientific movements arise and develop. It has obvious utility and is familiar to all of us, if not under that title. The "Matthew effect" to which he also refers is more contentious because it implies, without openly stating, that those who are not members of the dominant school are discriminated against in the competition for research funds and publication in prestigious journals. It would be idle to pretend that personal considerations never influence the decisions of editors or grant-giving bodies, but intellectual considerations are probably more important than personal rivalries in favoring those who subscribe to the dominant paradigm. Those whose ideas are out of tune with the spirit of the times are always at a disadvantage. I would guess that on the whole the effects are beneficial, though undoubtedly men who are ahead of their time get less than their due as a result. Indeed, for a long time this is what happened to Eli Robins and his colleagues.

Those who are out of sympathy with the aims and philosophy of the neo-Kraepelinian school can console themselves with two thoughts. Its present dominance will not last forever, or even for long if it commits itself to a crude belief in discrete disease entities and ignores the effects of social and psychological influences. And if their own research is really important, it will not languish forever in minor journals. Like the Abbé Mendel's genetic researches, it will eventually be recognized. I hope, though, that it will be possible for everyone with an interest in clinical research to accept the need for operational definitions of diagnostic and other key technical terms without feeling that by doing so they are subscribing to an alien ideology. For my own part I regard the publication of the Feighner criteria as a major technical advance, but that does not mean that I regard myself as a "neo-Kraepelinian," or subscribe to all of the nine tenets to which Blashfield refers.

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A Client Outcome Planning Model for Assessing Psychiatric Rehabilitation Interventions

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Abstract

Skill training, drug therapy, and community support strategies are the three primary intervention techniques used by practitioners attempting to rehabilitate severely psychiatrically disabled clients. The present article describes a comprehensive client outcome planning model that encompasses both the intended and unintended effects of an intervention, and that extends beyond such traditional outcome measures as recidivism, clinical relapse, and employment. In addition, data collection strategies and instruments capable of measuring a broad range of possible outcomes are described. A comprehensive model has the advantage of encouraging researchers to consider, during the process of research design, the specific outcomes that will and will not be effected by an intervention. Furthermore, such a model discriminates between process and outcome variables, limits the scope of the implications derived from the research data, and encourages the researcher to assess both the positive and negative effects of the rehabilitation intervention.

There have been a number of studies assessing the efficacy of rehabilitation programs for persons with severe psychiatric disabilities over the last two decades. The first overview of the effectiveness of the field of psychiatric rehabilitation focused on studies undertaken primarily in the 1960s (Anthony et al. 1972). Subsequent reviews covered additional investigations conducted during the 1970s (Erickson 1975; Bachrach 1976; Anthony, Cohen, and Vitalo 1978). In addition to these general overviews, there have been reviews of outcome in specific psychiatric rehabilitation and community support settings—for example, community residential facilities (Goldmier 1977; Carpenter 1978); halfway houses (Cometa, Morrison, and Zishoren 1979); and day hospitals (Moscowitz 1980). Still other reviews have assessed the effectiveness of various skill training approaches (Anthony and Margules 1974; Hersen and Bellack 1976; Anthony 1979; Wallace et al. 1980); drug therapy, alone or in combination with psychosocial rehabilitation (Tobias and MacDonald 1974; Engelhardt and Rosen 1976; Gardos and Cole 1976; Goldberg et al. 1977; Davis et al. 1980); and the major community intervention approaches (Test and Stein 1978).

Essential Rehabilitation Ingredients

The research of the last several decades has focused on three major contributors to client rehabilitation outcome variance:

- Skill training interventions, which teach the client skills necessary for success in a particular environment.
- Drug therapy interventions, which reduce symptomatology and prevent relapse.
- Community support interventions, which enhance the client's

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ability to function in specific community settings.

These three interventions are the treatment modalities that a psychiatrically disabled client will most typically experience (exclusive of custodial care).[1] Although the focus of a research study may be on one particular intervention strategy, a researcher must control for the fact that a client is often concurrently receiving one or both of the other interventions. All three types of interventions are known to contribute to some of the same measures of rehabilitation outcome (Anthony 1979).

Traditional Outcome Assessments

Early studies of psychiatric rehabilitation relied almost exclusively on recidivism, relapse, and, to a lesser extent, employment data as outcome criteria (Anthony et al. 1972; Mosher and Keith 1979). Although these measures have undeniable advantages—they are easily objectified, are readily understood by lay people, imply tangible economic benefits, and make it possible to compare studies using similar outcome measures— the importance of using a broader range of outcome measures has been stressed repeatedly (Anthony et al. 1972; Erickson 1975; Bachrach 1976; Anthony, Cohen, and Vitalo 1978; Mosher and Keith 1979).

Need for a Comprehensive Outcome Model

Lacking a comprehensive outcome assessment model, rehabilitation planners and policy makers tend to think of their interventions as having an impact only on the outcome goal of immediate interest to them. Concern with the attainment of treatment objectives often obscures the importance of investigating other potential outcomes. For example, the deinstitutionalization process has been successful in reducing the number of clients residing in state hospitals, but planners ignored other outcome goals such as clients' "quality of life." Thus, while the goal of deinstitutionalization was achieved, it was seemingly done at the expense of other outcomes that were not even considered in the initial planning process. An overall assessment model would provide policy makers with an overview of the many effects on clients of potential program and policy changes.

An outcome assessment model can also heighten treatment practitioners' awareness of the intended *and* unintended effects of their clinical interventions—effects that can be positive or negative. For example, clients' reports of a successful vocational rehabilitation intervention might be correlated with clients' reported satisfaction with their living situation (Anthony 1980). Or, a drug therapy intervention, while decreasing symptomatology, could decrease the client's physical fitness and energy level so as to interfere with vocational training (Anthony 1979).

In addition, an outcome assessment model is a useful planning guide. Researchers must ensure that their experimental designs and procedures provide for an evaluation of the total impact of the intervention. At the present state of knowledge, it is difficult to make assumptions about the potential effects of an intervention. For example, measures of client vocational change are often uncorrelated with measures of change in psychosocial functioning (Bolton 1974, 1978; Growick 1979). It behooves researchers, therefore, to generate hypotheses based on the full range of outcome variables that might be expected to change in a positive or negative direction.

The assessment model presented here is designed to assist researchers in generating the types of outcome data needed by policy makers and practitioners. It is based on two assumptions:

- Change on a single measure of client outcome does not indicate that seemingly related measures of change have also been affected (Bolton 1978). Therefore, to the extent possible, within the obvious limits of the researcher's resources, a range of outcome variables should be studied.
- A positive effect on one client outcome measure may have an associated negative effect on other measures. Therefore, the researcher must be alert to the possible adverse effects of his intervention. For example, Vitalo (1971) reported that his experimental group surpassed the control group in targeted interpersonal skills but was also rated as more anxious.

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[1] Two other interventions, psychotherapy and family treatment, have been used and researched less often. Psychotherapy research with severely disabled clients was on the wane during the 1970s (Mosher and Keith 1979), whereas family treatment (albeit with a less dynamic and more supportive-educational approach than formerly) attracted renewed research interest (Anderson, Hogarty, and Reiss 1980).

Differentiating Process From Outcome

Before a comprehensive client outcome assessment model relevant to all types of rehabilitation interventions is examined, an important distinction in skill training research should be emphasized: the difference between process and outcome measures. The outcome assessment model encourages the researcher to collect certain common measures of the training *process* as well as the training *outcome*. The description of key ingredients of the training process allows for more careful replication of the intervention. Additionally, process assessments, particularly measures of skill acquisition, ensure that an intervention did in fact occur—there are examples in the literature of failure to acquire skills following skill training. If skill acquisition does not occur, the anticipated independent variable is missing, and thus inferences about skill training effects made from outcome assessment are meaningless.

Table 1 identifies some of the basic elements necessary to describe a skill training intervention. This information is in addition to the required description of such client characteristics as age, sex, psychiatric diagnosis, and functional rehabilitation diagnosis. All skill training intervention programs are not alike, just as all halfway houses are not alike. Significant learning for policy makers, researchers, and clinicians can occur only if details of the training process which produced a certain outcome are specified. Even when the researcher has analyzed outcomes compre-

Table 1. Assessments of the skill training process

	Process categories			
	Client involvement	**Client understanding**	**Client skill acquisition**	**Client change in training setting**
Definition	Criteria indicative of client's willingness to participate in the skill training process	Criteria indicative of client's knowledge of what is meant by each skill and agreement that the skill is important to learn	Criteria indicative of the client's performance of the skills in the training environment, pre- and posttraining	Criteria indicative of client adjustment (exclusive of the targeted skills) in the training or treatment environment, pre- and posttraining
Examples of measures	Percent of training sessions attended Percent of homework assignments completed on time Client level of self-exploration before or during training Ratings of client "attending skills" during training Description of procedure for allowing client absence from training	Client sign-off that skill is important to learn Client's ability to define the skill that he or she is trying to learn Client can state why skill is important to learn Client ranks the skill to be learned as one of the most important skills to be learned	Client pre-posttraining skill level change as measured in the training setting. Observed and measured, e.g., by paper and pencil tests, audio or videotape, ratings by experts on skill behavior, role plays, and simulations	Client pre-post change as measured in the training or treatment setting. Ratings and scores of overall functioning, symptomatology, and adjustment obtained from observations of behavior in the treatment/training setting.
Training program description	Source where additional information about the training procedures can be obtained. Source may be either the present research article or another available source (published or unpublished). The actual training program is detailed with respect to the training content, demonstrations, practice sessions within and outside of training, homework assignments, use of other concurrent interventions, trainer experience, and skill level.			

hensively and specifically, without an accurate and understandable process description, the relevance of findings to possible treatment and policy changes is likely to be obscured.

The process categories in table 1 are essential dimensions for a researcher to report, but the degree to which they are described in the literature is highly variable. For example, skill training programs differ widely in the degree of *client involvement*. The element of choice to become or stay involved in the training process is a significant variable that needs to be described.

Client understanding is another element that is stressed more in some programs than in others. In an ideal training situation, clients would know exactly what skill they were learning and why, and would have expressed a particular desire to learn it. Of course, most studies of skill training are instances of group skill training. Unless great care is taken in the formation of the groups, a certain percentage of group members may not know exactly what skill they are learning, know why it is important, or believe it to be valuable to them. While group training of severely psychiatrically disabled clients may inevitably be somewhat deficient in the area of client understanding, it is important for researchers to report on the magnitude of this deficiency.

An example of a group training program that was tailored to clients' needs has been reported by Chaney, O'Leary, and Marlatt (1978). In this study, participants not only learned problem-solving skills for prepared situations but also were given practice in dealing with problematic situations in their own lives. Another study (Vitalo 1979) maximized client understanding by using an individual rather than a group approach. Each participant's specific skill needs were individually assessed, and training on those skills most important to the client's life circumstances was provided.

Data with respect to *skill acquisition* are obviously of greatest importance. If there are no significant pre-post training changes on targeted skills, then the study lacks its intended independent variable.

The fourth dimension, *client change in training setting*, includes measures taken within the training setting or time period. These assessments differ from skill acquisition measures in that they do not specifically assess the targeted skill; instead, they reflect a more global assessment of the client's functioning—overall adjustment, symptomatology, or nontargeted skills. Examples of instruments commonly used to assess client change in the treatment setting are the Brief Psychiatric Rating Scale, Nurses' Observation Scale for Inpatient Evaluation, Present State Examination, and simulations or role plays of skills not specifically targeted for training. Because these assessments are made within the training setting or period, they should be viewed as process measures.

It is hypothetically possible to observe client change in the training setting without an accompanying skill acquisition change. The very process of being engaged in an interpersonal skill learning activity might be enough to affect the more global ratings of a client's adjustment without corresponding significant effects on skill acquisition measures.

The final chart entry in table 1, *training program description*, serves as a reminder that a detailed account of the training intervention should be available. A reference in the research report should indicate from whom or where this description can be obtained.

There are several important distinctions between the process phase of assessment and more traditional measures of skill training outcome. Most importantly, measures of clients' ability to demonstrate targeted skills *during the training experience* are viewed as process measures—not measures of outcome. Skill acquisition measures do not indicate whether generalization to the environment of need has occurred. Studies which use acquisition measures as the primary dependent variables are actually studies of the skill training process. While such explorations of the critical ingredients of the skill training process (e.g., Eisler et al. 1978) are valuable, they should not be confused with skill training outcome studies. Similarly, such measures as the clients' ability to perform skill training homework assignments are viewed in this model as process rather than outcome measures. A favorable outcome is considered to have occurred when the client performs the skills outside the context of the training situation.

The intent of table 1, however, is not to define arbitrary categories or to encourage semantic arguments over what a "real" outcome is. The categories have heuristic value and are not necessarily discrete entities. For example, if a client acquires the skill of "following directions" during her sheltered workshop training experience, applies the skill within the training setting (in this case, the sheltered workshop), and, as a result, receives higher ratings from her sheltered workshop supervisor—is that not client outcome? If the client's goal is to work successfully in a sheltered workshop environment, then these process goals are also outcome goals. However, the planning model does encourage researchers and evaluators to consider benefits that extend beyond the immediate effects of specific interventions.

A Comprehensive Outcome Assessment Planning Model

The desired outcome of rehabilitation, be it physical or psychiatric, is to help the client to perform those physical, emotional, and intellectual skills necessary to function in his or her own unique living, learning, and working environment, with the least amount of help necessary from agents of the helping professions (Anthony 1977).

As shown in table 2, there are essentially two types of rehabilitation outcome categories:

- Client skill application— assessments which indicate that the client is performing certain skills in the environment of need.
- Client benefits—assessments which measure the expected results of the intervention and the degree to which client goals (desire to live in a community residence, return to school, obtain work in a sheltered workshop, or reduce maintenance medication) have been realized.

The distinction between client skill application and client benefits is an important one, analogous to the distinction between client skill acquisition and client skill application. Measures of client skill application document that the client's observable performance of skill within a particular environment has changed. Measures of client benefits document the benefits which the client is now receiving from a rehabilitation intervention.

For example, an adolescent client's difficulty in paying attention in the classroom is contributing to her poor grades. After a change to a less demanding and more supportive learning environment, the client can *apply* her "attending skills" in the classroom environment so that she *benefits* by earning a passing grade. Another example might be a client whose uncontrollable temper portends failure for his efforts to remain in a halfway house setting. After training in self-control, the client can *apply* his skills in the residential environment so that he *benefits* by being able to live for an entire year in the halfway house setting. A final example is a client who is too symptomatic to interview for a job and thus will not seek part-time employment. After drug treatment, the client can *apply* her existing job interview skills in an employment interview so that she *benefits* by obtaining a part-time job.

The *raison d'être* for a rehabilitation intervention is the belief that the learning of certain skills, the taking of medication, and the provision of a supportive system will somehow improve or benefit the clients' functioning in certain environments. Thus, research investigations assess whether improvements in the clients' living, learning, or working situation have occurred as a result of the rehabilitation intervention. Concurrently, skill application is assessed to determine whether the rehabilitation intervention has improved the client's ability to perform in the needed environment. Thus, in a thorough investigation of a rehabilitation intervention, both types of outcome assessments—client skill application and client benefits—are needed.

For example, long-term research into support systems suggests that while a support system provides benefits to a client, it may not increase the client's skills (Pasamanick, Scarpitti, and Dinitz 1967; Davis, Dinitz, and Pasamanick 1972). Likewise, while drug therapy may benefit the client by forestalling relapse and

Table 2. Assessments of rehabilitation outcomes

Outcome categories:	Client skill application			Client benefits
	Physical	Emotional	Intellectual	
Outcome environments:				
Living				
Learning				
Working				

reducing symptomatology, it cannot be assumed that it has a positive impact on the client's skills (Engelhardt and Rosen 1976). Indeed, researchers may wish to investigate whether drug treatment has a negative effect on certain client skills.

The purpose of table 2 is to guide researchers in their development of an outcome assessment procedure appropriate to the rehabilitation intervention under investigation. Several components deserve emphasis. Outcome environments are subdivided into living, learning, and working environments to ensure that the specific skill application environment of need is identified, as well as the environment in which the expected benefits will accrue. The categories of living, learning, and working encompass the entire universe of client skill application settings and potential benefits. As such, the categories encourage the researcher to analyze the total impact of a rehabilitation intervention. At the same time, however, these categories also encourage the researcher to identify the specific environmental impact of the intervention. For example, in a skills training intervention designed to train punctuality skills, the researcher should know beforehand if the client is expected to apply skills in a living environment (arrive on time for meals), a learning environment (arrive on time for class), or a working environment (arrive on time for work). Likewise in the client benefits category, it should be considered whether the application will result in a benefit in the living environment (ability to live at home), learning environment (ability to remain in school), or working environment (ability to remain employed).

The living, learning, working categorization assists the researcher to think comprehensively in the initial planning process about the variety of environmental applications and benefits. Having initially considered this broad perspective, the researcher can then move on to specify exactly what environments are included in the research design. The planned omission of the other environments correctly limits the implications of the research results to the environment in which assessments occurred.

The subdivision of client skill applications into physical, emotional, and intellectual categories serves much the same purpose; it broadens the researcher's perspective so that the universe of client skill outcomes is considered. *Skill training need not be limited to training in social or job skills.* The needs of the client are much broader, and the technology of skill training can be applied to physical, emotional, and intellectual goals.

To train clients only in social (emotional) skills when they might just as urgently need training in physical fitness, for example, is not only clinically questionable but also problematic from the standpoint of research design. Indeed, physical skill is an area of functioning that has traditionally been ignored in psychiatric treatment. Yet the physical dimension is an area in which clients are often deficient, and which by virtue of its concreteness, may provide generalizations to other areas of functioning (Vitalo and Farkas 1979).

Having considered the universe of possibilities in planning an intervention strategy, the researcher then specifies exactly what types of applications and benefits are to be investigated. For example, the client's application of physical skills (e.g., fitness and nutrition) in the living environment may be studied to ascertain whether it benefits the client's living environment (reduced level of medication), learning environment (improved school attendance), or working environment (higher ratings by vocational workshop supervisor). Note that in this hypothetical example the physical skill application is studied with respect to its effects on the client's living, learning, and working environments.

The initial categorization process is not intended to generate arguments over whether a skill application is "really" physical, emotional, or intellectual. Its purpose is simply to encourage researchers to think expansively of the types of skill applications that might be affected by the intervention before identifying those of immediate research interest. Because an intervention might have both positive and negative effects, researchers need to consider a number of potential outcome assessments before specifying the particular measures to be used. The use of table 2 in the research planning and design process can help to ensure that the final outcome assessment procedure is thorough as well as specific.

One other point deserves emphasis with respect to the benefits category of table 2. Researchers must be encouraged to include as dependent variables direct measures of real life client change that are easily understood by lay persons (e.g., consumers, significant others, taxpayers, politicians). Examples might be an increased number of friends (living environment), a high school diploma (learning environment), or a move from a sheltered employment setting to a competitive employment setting (working environment). As can be seen from table 3, some of these direct benefits are environmentally specific, while others can be adapted to any environment. For example, client satisfaction measures can be obtained with respect to the client's living, learning, or working environment. In contrast, the percentage of clients maintaining employment is obviously a benefit criterion specific to the working environment.

Each of the measures listed in table 3 is a potential outcome benefit of rehabilitation. Researchers must decide in the planning process which type of benefits to include in their investigation. The benefits that are studied will no doubt vary over time. Recent interest, for example, has focused on the impact of skill training on symptomatology (Eisler et al. 1978; Vitalo and Ross 1979; Wallace et al. 1980) and the possible interaction between skill training and drug treatment (Goldberg 1980).

Table 3. Examples of direct client benefit measures related to specific environments

Living environment

Recidivism percentage decreased
Length of time in residence appropriate to residential needs of the client
Number or type of leisure activities increased
Improved ratings by significant others in client's residence
Economic support from others decreased

Learning environment

Attendance percentages increased
Improved grades
improved ratings of adjustment by teacher
Credits or diploma earned

Working environment

Increased percentage of trainees obtaining employment
Increased dollars earned
Increased number of days per month worked
Improved ratings by work supervisor
Increased percentage of trainees maintaining employment

Benefits capable of being measured in any environment

Symptom reduction
Client satisfaction
Medication reduction
Disciplinary measures decreased
Increased interpersonal interactions
Clinical relapse delayed

Currently Available Rehabilitation Outcome Instruments

This section presents a description of outcome measurement instruments used in skill training, drug therapy, or community support intervention research. It is not an exhaustive review of all measures. The instruments included have been standardized to a certain extent and have been mentioned at least once in the skill training literature or in reviews of drug therapy and community support interventions. Personal communication with investigators conducting research into the outcome of rehabilitation efforts with the chronically disabled has identified additional and/or unpublished measures that appear to be useful in describing skill acquisition, skill application, or client benefits such as symptom reduction or client satisfaction.

The following types of outcome measurements have been excluded from this review:

- Instruments used in outcome research generally, but not in research on the rehabilitation of the chronically disabled specifically (see Waskow and Parloff 1975 for review).
- Specialized assessment techniques used exclusively in strictly behavioral token economy studies (see Wallace, in press, for review).
- Rating scales used with the chronically disabled but not reported in the skill training, community support, or drug therapy literature (see Goldberg 1974 for review).

The difficulties encountered in attempting a comprehensive search of available outcome measures are in many ways similar to those that confront a researcher in trying to select an appropriate outcome measure. Many measures, particularly those described in the social skill training literature, reflect molecular behavior. Moving from such measures as frequency counts of the number of eye contacts made in 3 minutes of conversation to the more complex assessment of social behavior involves a loss of clarity and specificity. Because the definition of social skills is usually vague (Alevizos and Callahan 1977; Trower, in press), it is often difficult to decide whether a particular measure is appropriate for other studies. Two common responses to this problem of vagueness have been either to concentrate on the further refinement of assessment of molecular behavior (Wallace et al. 1980) or to develop idiosyncratic measures for each new set of research problems. Idiosyncratic instruments are difficult for a potential researcher to use in a reliable replication. Due to journal space limitations, the instrument is often not described in sufficient detail. Many studies do not even reference the instruments that were used, making it more difficult to identify potential standardized measures.

Another problem is that reliability and validity measures are often not reported (Ciminero, Calhoun, and Adams 1977). Reliability tends to be more frequently reported than validity—perhaps reflecting the problems that arise in establishing convergent or concurrent validity for a vaguely defined set of complex behaviors (Alevizos and Callahan 1977). Indeed, the question of the validity of behavioral measures has rarely been considered (Wallace, in press). In the area of community adjustment measures, however, even formal tests of reliability are seldom conducted (Waskow and Parloff 1975). Many instruments used in outcome research were developed on acute inpatients or outpatients and then applied to the chronic population, for lack of a population-specific instrument. When the researcher moves beyond direct measurements of change (e.g., number of days attending a workshop) and applies assessment techniques standardized on other populations, problems with reliability and validity arise. Validity is also a problem in attempts to measure particular types of skill acquisition. The control of hallucinations or the reduction of other psychotic symptoms, which has typically been the focus of both drug and behavioral therapy studies, is difficult to measure directly. Although physiologic or self-monitoring measures have been described, little validity for these measures has been established (Alevizos and Callahan 1977).

Problems of reliability and validity become more complex when the question of skill application is raised. In personal communications, researchers were almost unanimous in calling for more measures designed to assess the generalization of skill acquisition. Hersen and Bellack (1977, p. 510) state that the "importance of generalization in most behavioral research has been acknowledged more in print than in actual practice." There is an acknowledged lack of a systematic framework in which to produce generalization techniques or measures that are ethical and naturalistic (Hersen and Bellack 1977; Curran, in press). Only 40 percent of studies targeting the skills behaviors of the chronically disabled addressed some aspect of the problem of skill application (Wallace, in press). In those studies that have addressed generalization, frequency counts of behaviors, and unstructured or structured questionnaires have typically been the assessment format used (Patterson and Teigen 1973; Tracy, Briddell, and Wilson 1974; Hollingsworth and Foreyt 1975).

Although some investigators have used standardized measures of skill application—for example, Edelstein and Eisler (1976), who studied the application of assertiveness training to items not included in the training curriculum—the research subjects were drawn from a less severely disabled population than the chronically disabled. The generalization of training to situations using confederates has been measured by Goldsmith and McFall (1975) in a landmark study of skill training. Validity and reliability studies are still being conducted on these instruments. Unfortunately, the number of raters (confederates and others) involved in Goldsmith and McFall's Confederate Test of Interpersonal Situation makes the instrument difficult to use in smaller scale research projects.

In addition to assessing whether the skills learned in training are applied in the targeted environment, there is a pressing need for the development of skill acquisition measures that positively correlate with direct measures of client benefits. Skill acquisition is often assessed by role play situations, but whether performance on these role plays is actually related to the current or subsequent attainment of client benefits is not generally known (Bellack, Hersen, and Lamparski 1979). Several studies on populations other than the chronically mentally disabled have reported correlations between role play assessments and delinquent behavior (Freedman et al. 1978) and between role play behavior and the subsequent drinking behavior of alcoholics (Chaney, O'Leary, and Marlatt 1978).

Predictive validity based on measures of inpatient behaviors has been reported by Redfield (1979) and Power (1979) using the Clinical Frequencies Recording System and the Time Sample

Behavioral Checklist. Both these instruments were developed and standardized in the decade-long investigation conducted by Paul and his associates. Predischarge scores on these instruments can significantly predict the discharged patient's functioning in the community (Paul, in press).

Tables 4 and 5 attempt to address the basic information needs of a potential researcher in the field of rehabilitation outcome. Instruments are first grouped according to the predominant focus of the item: skills (table 4) or client benefits (table 5).[2]

Secondly, instruments are categorized according to their environmental emphasis (living, learning, working). The skills or benefits focus of the items is then characterized as physical, emotional, or intellectual. This categorization is somewhat arbitrary and reflects the major domain in which the skill is exercised or the benefit realized. (An emotional skill of "temper control" may, of course, also have physical and intellectual components.) Measurements with a primary focus on client benefits are divided into those predominantly reflecting the benefit of symptom reduction or "other." Within the "other" category are included measures of client satisfaction, and measures related to frequencies (e.g., income levels, days in community) that may be included within a larger measure. Since the focus of tables 4 and 5 is on instruments, there is no listing of references which simply used frequency counts or percentages of a certain behavior (e.g., days hospitalized over a 6-month period).

Information about the person completing the assessment form or task is provided. Direct observations are labeled "practitioner" sources. This information is included because the vantage point of the evaluator has been a controversy. Although there are problems with self-report measures (Cartwright 1975), instruments that use the client as the source of direct information (particularly in the area of client benefits) have many advantages (Anthony, Cohen, and Vitalo 1978; Bigelow and Brodsky 1980*a*; Trower, in press).

The source of the instrument—the skill training (ST), drug therapy (DT), or community support (CS) literature—is specified. Instruments that were suggested in personal communications are labeled (PC). As the reliability and validity of such measures are often in question, the first column of tables 4 and 5 identifies references in which reliability and validity information is presented.[3] When reliability or validity is not directly reported, but alluded to in the literature consulted, a question mark (?) is indicated.

The population for which a measure is relevant is important in terms of its validity. Some measures have proven validity, but are now being extended to populations other than those for which they were originally intended. The dearth of instruments standardized on the chronic population has made it necessary to "borrow" instruments from studies of other groups. Many studies only indicate that a population is an "inpatient psychiatric population" and consequently leave the matter somewhat open to question. The column, *original population focus*, describes the group on which the validity data have been reported or the group studied when the original instrument was being developed. Question marks indicate that the general information is unspecified in the literature consulted. The references listed in the first column of tables 4 and 5 are, as often as possible, the primary source for that instrument. Otherwise, the reference reflects a discussant article. The references in parentheses in the first column of tables 4 and 5 provide additional information about the instrument. Additional references are provided when reliability or validity has been clearly discussed by someone other than the primary source author.

In summary, the process of attempting to gather information about the available instruments in the field of rehabilitation outcome assessment of the chronically disabled has indicated the following: (1) There is a lack of specificity in the description of instruments used, the population for which they are appropriate, their validi-

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[2] A number of measures assessing overall client needs are included, although, strictly speaking, they do not fall into the category of a specific treatment outcome assessment. Several Departments of Mental Health are currently developing statewide needs assessments that do focus on the general target of measurement reflected in tables 4 and 5—that is, on client skills and benefits. The measures included here are provided to demonstrate ways in which this topic is being researched on a broader scale.

[3] For some instruments, reliability and validity studies are presently being conducted to augment those already done or to confirm preliminary results; this distinction is not made.

Table 4. Skills measures

	Item focus				Completed by:						Orig pop focus			
			Benefits											
Instrument	Envir	Skills	SX reduc	Other	Client	Sig other	Prac confed	Cited in	Rel	Val	In-pt	Out-pt	Other	Additional description
Global assessment														
Level of Functioning Assessment (New Jersey) New Jersey Division of Mental Health and Hospitals (1979)	Liv Work	E/P	E				X	PC	?	?	X			5-point scale, administered 7 days after admission, 30 days after admission, and in community settings every 90 days. Self-maintenance, social functioning community living skills.
Multifunction Assessment Instrument (Rhode Island) Angelini, Potthof, and Goldblatt (1980)	Liv Ln Work	P/E I	E	P/E			X	PC	?	?	X			Broad needs assessment, ranging from items for inpatient to independent living.
Needs Assessment Instrument (Michigan) Cornhill Association (1980)	Liv Work	P/E	P/E	P/E			X	PC			X			Not treatment instrument, but planning tool; used in Northampton, Mass., and State of California. 111 items: functional status service needs.
Emotional functioning														
Behavior Assertiveness Test (BAT-R) Eisler, Hersen, and Miller (1976)	Liv	E					X	ST	X	X		X		Standardized interpersonal situations. Assess discrete behaviors.
Confederate Generalization Test of Social Skills Liberman et al. (1978) (Liberman et al. 1979)	Liv	E		E	X		X	ST			X			Series of behavior ratings; generalization to new situations and new confederates; measures skills and comfort in interaction.
Extended Interaction Test Goldsmith and McFall (1975)	Liv	E			X		X	ST			?	?		Test of generalization of social skill interaction with confederate in 2 situations—interpersonal skill.
Human Relations Scale (Carkhuff 1969)	Liv Ln Wk	E					X	ST	X	X			X	5-point scale measuring clients' ability to communicate empathic understanding.

Note.—Abbreviations used in table headings: Envir, Environment; SX reduc, Symptom reduction; Sig other, Significant other; Prac confed, Practitioner/confederate; Rel, Reliability; Val, Validity; Orig pop focus, Original population focus for instrument development; Inpt, Inpatient; Outpt, Outpatient. **Abbreviations used in table text:** Liv, Living environment; Ln, Learning environment; Work, Working environment; P, Physical; E, Emotional; I, Intellectual; ST, Skills training literature; CS, Community support literature; DT, Drug therapy literature; PC, Personal communication.

Table 4. Skills measures—*Continued*

		Item focus												
			Benefits		Completed by:						Orig pop focus			
Instrument	Envir	Skills	SX reduc	Other	Client	Sig other	Prac confed	Cited in	Rel	Val	In-pt	Out-pt	Other	Additional description
Emotional functioning—continued														
Impact Message Inventory Kiesler et al. (1976)	Liv	E		E		X		ST	?	X			X	Rating of impact of social interaction, items reflect scales—dominance, hostility, etc.
Interpersonal Behavior Role-Playing Test Goldsmith and McFall (1975)	Liv	E					X	ST				X		25 tape-recorded role-played responses. Patient responses scored 0–2.
Interpersonal Situation Inventory Goldsmith and McFall (1975)	Liv	E					X	ST				X		Role-played items: meeting, talking to people, future ability; 5-point ratings.
Lawrence Interpersonal Behavioral Test Percell, Berwick, and Beigel (1974)	Liv	E					X	ST	?	?			?	Ratings of assertiveness, empathy.
Minimal Social Behavior Scale Farina, Arenberg, and Guskins (1957)	Liv	E					X	ST	X	X	X			Retrospective; 32 items, social situation; structured interview.
Occupational Skills Assessment Matthews (1980)	Work	E					X	PC	?	X				13 situations (job-seeking, job-holding)—role-play simulations.
Patient Activity Checklist Aumack (1969)	Liv	E	E				X	ST	X		X			24 behavior categories of inpatients in dayroom.
Rathus Assertiveness Schedule Rathus (1973)	Liv	E					X	ST	X	X		X		
Simulated Social Interaction Test Curran (1981) (Monti et al. 1980)	Liv	E					X	ST	X	X	X	X	X	Generalization of social skills and anxiety.

Note.—Abbreviations used in table headings: Envir, Environment; SX reduc, Symptom reduction; Sig other, Significant other; Prac confed, Practitioner/confederate; Rel, Reliability; Val, Validity; Orig pop focus, Original population focus for instrument development; Inpt, Inpatient; Outpt, Outpatient. **Abbreviations used in table text:** Liv, Living environment; Ln, Learning environment; Work, Working environment; P, Physical; E, Emotional; I, Intellectual; ST, Skills training literature; CS, Community support literature; DT, Drug therapy literature; PC, Personal communication.

Table 4. Skills measures—*Continued*

	Item focus													
			Benefits		Completed by:						Orig pop focus			
Instrument	Envir	Skills	SX reduc	Other	Client	Sig other	Prac confed	Cited in	Rel	Val	In-pt	Out-pt	Other	Additional description
Emotional functioning -continued														
Work-Related Productive Activity Neuhring, Snyder, and Ladner (1979)	Work	E		E	X		X	CS				X		Identifies type of work activity done and most liked or disliked/difficult aspect.
Intellectual/multiple areas of functioning														
Adaptive Behavior Scale Nihira, Foster, and Spencer (1968)	Liv	E/P	E				X	PC	X		X			Normed on MR populations; used to describe chronic psychiatric patients—not treatment instrument.
Behavior Observation Inventory Alevizos et al. (1978)	Liv	E/P	E				X	ST	X		X	X		16 behavior categories, time sampling, used inpatient and outpatient.
Behavior Performance Tests Alevizos and Callahan (1977)	Liv	E/P	E/P				X	ST			X			Aggressive behavior, unusual behavior, self-care, work, verbal interaction.
Clinical Frequencies Recording Systems Redfield (1979)	Liv	P/E	E				X	ST	X	X	X			Rate/opportunity of particular behaviors, inpatient setting; 4 classes: service utilization, inappropriate time, destructive behavior, patient responsiveness.
Inpatient Scale of Minimal Functioning Paul et al. (1976) (Paul, Redfield, and Lentz 1976)	Liv	E/P	E					PC		X				Revision of Social Breakdown Syndrome Gradient Index.

Note.—Abbreviations used in table headings: Envir, Environment; SX reduc, Symptom reduction; Sig other, Significant other; Prac confed, Practitioner/confederate; Rel, Reliability; Val, Validity; Orig pop focus, Original population focus for instrument development; Inpt, Inpatient; Outpt, Outpatient. **Abbreviations used in table text:** Liv, Living environment; Ln, Learning environment; Work, Working environment; P, Physical; E, Emotional; I, Intellectual; ST, Skills training literature; CS, Community support literature; DT, Drug therapy literature; PC, Personal communication.

Table 4. Skills measures—*Continued*

	Item focus				Completed by:						Orig pop focus			
			Benefits											
Instrument	Envir	Skills	SX reduc	Other	Client	Sig other	Prac confed	Cited in	Rel	Val	In-pt	Out-pt	Other	Additional description
Intellectual/multiple areas of functioning—continued														
Nurses Observation Scale of Inpatient Evaluation (NOSIE-30) Honigfeld and Klett (1964) (Honigfeld 1966)	Liv	E/P	E				X	ST	X	X	X			6 factor scales; social competence, personal neatness, manifest psychosis. Rated over 3 days by nurses.
Occupational Therapy Trait Rating Scale Clark, Koch, and Nichols (1965)	Work	P/E	E/P				X	ST	X	X	X			Behavioral trait scale based on sheltered workshop population.
Problem Solving Scale (Valle 1975)	Liv Ln Wk	I				X		ST	X	?			X	5-point scale measuring client's ability to generate alternatives, weigh values, and make a decision (as described by Carkhuff 1969).
Program Development Scale (Valle 1975)	Liv Ln Wk	I					X	ST	X	?			X	5-point scale measuring client's ability to develop systematic steps to reach observable goal (as described by Carkhuff 1969).
Social Breakdown Syndrome Gradient Index Gruenberg, Brandon, and Kasius (1966)	Liv	E/P	E					PC	X		X			Questionnaires; staff rates frequency of behavior, inpatient setting.
Time-Sample Behavioral Checklist Power (1979)	Liv	P/E	E				X	ST	X	X	X			Behavior items: awake-asleep, crazy behaviors, concurrent activities. Predictive validity of significant release.
Vocational Behavior Checklist Walls, Zane, and Werner (1979)	Work	P/E					X	PC	X	X			X	Prevocational skills, job-seeking, interviewing, union skills; 339 skill items.

Note.—**Abbreviations used in table headings:** Envir, Environment; SX reduc, Symptom reduction; Sig other, Significant other; Prac confed, Practitioner/confederate; Rel, Reliability; Val, Validity; Orig pop focus, Original population focus for instrument development; Inpt, Inpatient; Outpt, Outpatient. **Abbreviations used in table text:** Liv, Living environment; Ln, Learning environment; Work, Working environment; P, Physical; E, Emotional; I, Intellectual; ST, Skills training literature; CS, Community support literature; DT, Drug therapy literature; PC, Personal communication.

Table 4. Skills measures—*Continued*

		Item focus									Orig pop focus			
			Benefits		Completed by:									
Instrument	Envir	Skills	SX reduc	Other	Client	Sig other	Prac confed	Cited in	Rel	Val	In-pt	Out-pt	Other	Additional description
Intellectual/multiple areas of functioning—continued														
Work-Behavior Coding System Tarlow and Alevizos (1975) (Ciminero 1977)	Work	P/E	E				X	ST			X			Muiticategory observation coding. Items: verbal interaction, aggression, unusual behavior, tasks. Subscale of Behavior Performance Test.
Work Behavior Questionnaire Tarlow, Alevizos, and Lafey (1975) (Ciminero 1977)	Work	P/E					X	ST	?	X	X			Staff circle "true" for work performance behavior.

Table 5. Benefit measures—*Global assessments*

Instrument	Envir	Skills	SX reduc	Other	Client	Sig other	Prac confed	Cited in	Rel	Val	In-pt	Out-pt	Other	Additional description
Community Adaptation Schedule Roen and Burnes (1968) (Cook and Josephs 1970)	Work Ln Liv			E/I	X			ST	X	?		X	X	Actual behaviors, feelings, beliefs, 240 items; may be inappropriate for hospital inpatients.
Community Adjustment Profile Evenson (1974)	Liv Work		E	E		X		ST	X	X	?	?		Designed using individual as own control; satisfaction with life in general.
CSP-Assessment Instrument Neuhring, Snyder, and Ladnor (1979)	Liv Work	E/P	E	E/P			X	CS	?	?	?	?		1–5 scale—Quality of Life score. Being developed by Fellowship House; items: use of community resources, independent functioning, social adjustment, work activities.
Fairweather Scale Fairweather et al. (1960)	Live Work	E/P		P/E		X		CS	?	?	X			General items assessing employment, rehospitalization, antisocial behavior, number of friends.

Note.—Abbreviations used in table headings: Envir, Environment; SX reduc, Symptom reduction; Sig other, Significant other; Prac confed, Practitioner/confederate; Rel, Reliability; Val, Validity; Orig pop focus, Original population focus for instrument development; Inpt, Inpatient; Outpt, Outpatient. **Abbreviations used in table text:** Liv, Living environment; Ln, Learning environment; Work, Working environment; P, Physical; E, Emotional; I, Intellectual; ST, Skills training literature; CS, Community support literature; DT, Drug therapy literature; PC, Personal communication.

Table 5. Benefit measures—*Continued*

Instrument	Item focus				Completed by:						Orig pop focus			
			Benefits											
	Envir	Skills	SX reduc	Other	Client	Sig other	Prac confed	Cited in	Rel	Val	In-pt	Out-pt	Other	Additional description
Global assessments—continued														
Global Assessment Scale Endicott, Spitzer, and Fleiss (1976)	Liv Ln	I	E		X	X	X	PC CS	X	X	?			Items: behavior disorganization, symptom dimension.
Oregon Quality of Life Questionnaire Bigelow and Brodsky (1980a)	Liv Work			E	X			PC CS	X	X	X			Structured questionnaire; trained interviewers; under study.
Personal Adjustment and Role Skills Ellsworth (1979) (Ellsworth 1975)	Liv Work	E	E	P/E		X		ST	X	X				Items related to: employment, unacceptable behavior, friendship skills, organization, confusion.
Self-Assessment Guide Willer and Biggin (1974) (Willer and Biggin 1976)	Liv Work		P/E	P/E	X			PC	X	X	X			Normed on acute inpatient; predictive of community tenure; satisfaction in seven areas of competence, assessed by patient.
Social Adjustment Inventory Berger et al. (1965)	Liv Work	E/P	E	E		X		CS	X	?		X	X	Family and social adjustment, social productivity, self-maintenance.
Social Adjustment Scale II Schooler, Hogarty, and Weissman (1979)	Liv Work	P/E		P/E			X	DS	X			X		Draws on client and significant others' perspective for item clusters: e.g., work roles, sexual adjustment, household concerns, romantic involvement, self-care, grooming.
Structured and Scaled Interview to Assess Maladjustment Gurland et al. (1972)	Liv Work	E		P/E			X	ST	X	X	X			8-point scales; work, family, social anxiety, self-image; structured interview.

Note.—Abbreviations used in table headings: Envir, Environment; SX reduc, Symptom reduction; Sig other, Significant other; Prac confed, Practitioner/confederate; Rel, Reliability; Val, Validity; Orig pop focus, Original population focus for instrument development; Inpt, Inpatient; Outpt, Outpatient. **Abbreviations used in table text:** Liv, Living environment; Ln, Learning environment; Work, Working environment; P, Physical; E, Emotional; I, Intellectual; ST, Skills training literature; CS, Community support literature; DT, Drug therapy literature; PC, Personal communication.

Table 5. Benefit measures—*Continued*

	Item focus				Completed by:						Orig pop focus			
			Benefits											
Instrument	Envir	Skills	SX reduc	Other	Client	Sig other	Prac confed	Cited in	Rel	Val	In-pt	Out-pt	Other	Additional description
Symptom reduction														
Behavioral Adequacy Scales Cartwright, Kirtner, and Fiske (1963)	Liv		E				X	ST	X	X		X		Items related to: contentment, confidence, attitudes to others; 14 scales.
Brief Psychiatric Rating Scale Overall and Gorham (1962)	Liv		E				X	ST DT CS	X	X	X			
California Psychological Inventory Gough (1948) (Gough, McClosky, and Meehl 1952)	Liv		E		X			ST				?	X	Dominance, assertiveness.
Client-Developed Self-Assessment Prager and Blum (1980)	Liv		E		X			PC	X	?	?	X		"Psychiatric young adults" norm. Items relate to: tension, self-image, depression; worth, semantic differential.
Fear Survey Schedule IV Wolpe and Lang (1964)	Liv		E		X			ST	X	X		X		122 items; used in assertiveness studies.
Fundamental Interpersonal Relationship Orientation —Behavior Schutz (1961) (Froehle 1970)	Liv	E	E		X			ST	X	X		?		Assess need for inclusion, control, affection—through behaviors (eye contact, leaning forward).
Hopkins Symptom Checklist Williams et al. (1968) (Derogatis et al. 1974)	Liv		E		X			ST	X	X		X		Estimates of symptom distress.
Inpatient Multidimensional Psychiatric Scale Lorr and Klett (1966) (Mariotto and Paul 1974)	Liv	I	E				X	ST CS	?	X	X			Items: excitement, retardation, cognition, distortion.

Note.—Abbreviations used in table headings: Envir, Environment; SX reduc, Symptom reduction; Sig other, Significant other; Prac confed, Practitioner/confederate; Rel, Reliability; Val, Validity; Orig pop focus, Original population focus for instrument development; Inpt, Inpatient; Outpt, Outpatient. **Abbreviations used in table text:** Liv, Living environment; Ln, Learning environment; Work, Working environment; P, Physical; E, Emotional; I, Intellectual; ST, Skills training literature; CS, Community support literature; DT, Drug therapy literature; PC, Personal communication.

Table 5. Benefit measures—*Continued*

	Item focus													
			Benefits		Completed by:						Orig pop focus			
Instrument	Envir	Skills	SX reduc	Other	Client	Sig other	Prac confed	Cited in	Rel	Val	In-pt	Out-pt	Other	Additional description
Symptom reduction–continued														
MMPI Dahlstrom, Welsh, and Dahlstrom (1972)	Liv		E		X			ST	X	X	X	X	X	Global disturbance.
Profile of Moods States McNair, Lorr, and Droppelman (1971) (Lorr, Daston, and Smith 1967)	Liv		E		X			ST	X	X		X		Adjective rating of moods by client; 5-point scale.
Psychiatric Status Schedule Spitzer et al. (1970)	Liv	E/P	E				X	ST	X	X	X	X		Role function impairment, ADL skills, general symptoms.
Psychotic Inpatient Profile Lorr and Vestre (1969)	Liv	E	E				X	ST	X	X	X			State hospital patient norms, bizarre speech, abusive behavior, etc.
Short Clinical Rating Scale French and Heninger (1970)	Liv		E				X	CS	X	X	X			
Taylor Manifest Anxiety Taylor (1953)	Liv		E		X			ST	X	X		X	X	225 items; correlates with physiological measures of anxiety.
Willner-Scheerer Test of Analogical Reasoning and	Liv Ln	I	I					DT	X	X	X			Focuses on cognitive slippage, associative focusing, abstraction. Discriminates functional disorders from organic.
Willner's Unusual Meanings Vocabulary Test Willner (1971) (Kiesler 1973)	Liv Ln	I	I				X	DT	X	X	X			

Note.—Abbreviations used in table headings: Envir, Environment; SX reduc, Symptom reduction; Sig other, Significant other; Prac confed, Practitioner/confederate; Rel, Reliability; Val, Validity; Orig pop focus, Original population focus for instrument development; Inpt, Inpatient; Outpt, Outpatient.
Abbreviations used in table text: Liv, Living environment; Ln, Learning environment; Work, Working environment; P, Physical; E, Emotional; I, Intellectual; ST, Skills training literature; CS, Community support literature; DT, Drug therapy literature; PC, Personal communication.

Table 5. Benefit measures—*Continued*

Instrument	Item focus				Completed by:						Orig pop focus			
			Benefits											
	Envir	Skills	SX reduc	Other	Client	Sig other	Prac confed	Cited in	Rel	Val	In-pt	Out-pt	Other	Additional description
Other assessments														
Community-Oriented Program Environment Scale Moos and Otto (1972)	Liv			E	X			CS	X	X		X		Same as Ward Atmosphere Scale—only for community programs.
Consumer Response Scale Segal and Aviram (1978)	Liv Work			E/P	X			PC	?	?	?	X		Patient satisfaction—living situation, therapy, leisure time.
Historical Information Form (Hargreaves et al. 1979)	Liv Wk	P/I		E/P	X	X	X	PC	X	X	X	X	X	Yields global score or longitudinal data for life table analysis; assesses need for institutionalization.
Katz Adjustment Scales Katz and Lyerly (1963)	Liv			E	X	X		DT ST CS	X	X	X			Taps differences in expectations; items: social behavior, free-time activities, satisfaction, and symptoms.
Normative Social Adjustment Scale Barrabee, Barrabee, and Finesinger (1955)	Liv			E/P			X							Information related to employment, economics, family life.
Self-Disclosure Scale Jourard (1971)	Liv			E	X			CS	X	?		X	X	Measures degree to which individual opens up in interaction.
Shipley-Hartford IQ Test Shipley (1946)	Liv Ln	I	I				X	ST DT						
Social Adjustment Scale Weissman, Paykel, and Siegel (1972)	Liv		E	E	X			ST	X	X	?	X		Used with acute psychiatric patients.
Tennessee Self-Concept Scale Ashcroft and Fitts (1964)	Liv			E	X			ST	X	X		?		

Note.—Abbreviations used in table headings: Envir, Environment; SX reduc, Symptom reduction; Sig other, Significant other; Prac confed, Practitioner/confederate; Rel, Reliability; Val, Validity; Orig pop focus, Original population focus for instrument development; Inpt, Inpatient; Outpt, Outpatient. **Abbreviations used in table text:** Liv, Living environment; Ln, Learning environment; Work, Working environment; P, Physical; E, Emotional; I, Intellectual; ST, Skills training literature; CS, Community support literature; DT, Drug therapy literature; PC, Personal communication.

Table 5. Benefit measures—*Continued*

	Item focus													
			Benefits		Completed by:						Orig pop focus			
Instrument	Envir	Skills	SX reduc	Oth-er	Client	SIG other	Prac confed	Cited in	Rel	Val	In-pt	Out-pt	Oth-er	Additional description
Other assessments–continued														
Treatment Effectiveness Scale Polak and Kirby (1976)	Liv			E	X	X	X	CS	X	X		X		Satisfaction with treatment. (A difficult instrument to obtain.)
Ward Atmosphere Scale Moos (1974)	Liv			E	X		X	CS	X	X	X			10 scales reflecting staff and patient perceptions of: support, staff control, autonomy, practical orientation encouraged.

Note.—Abbreviations used in table headings: Envir, Environment; SX reduc, Symptom reduction; Sig other, Significant other; Prac confed, Practitioner/confederate; Rel, Reliability; Val, Validity; Orig pop focus, Original focus for instrument development; Inpt, Inpatient; Outpt, Outpatient.
Abbreviations used in table text: Liv, Living environment; Ln, Learning environment; Work, Working environment; P, Physical; E, Emotional; I, Intellectual; ST, Skills training literature; CS, Community support literature; DT, Drug therapy literature; PC, personal communication.

ty, or the reference used to obtain the instrument itself. (2) There is a dearth of measures that have been standardized for the chronic population and that assess skill acquisition, application, or general benefits. Most instruments that relate to this population have been designed to tap benefits such as symptom reduction. (3) There are relatively few instruments assessing rehabilitation outcome that relate to drug therapy or community support programs (the latter being a relatively new and consequently somewhat limited research area). (4) Most drug studies rely on relapse rates or frequency counts of a specific behavior to measure their outcomes. (5) There are few instruments that directly assess client benefits using the client as a data source. (6) There are few instruments that assess skills or benefits gained in the learning environment.[4] (7) There are few instruments available that assess clients in the working environment. (8) There are few instruments that assess the skill application outcome of a skill training program; although simulated role plays have been used to assess skills, no instruments in the literature consulted have assessed generalization to the natural environment.

Rehabilitation Outcome Research: Some Conclusions

Client skill training research is analogous to the studies of counselor skill training carried out during the 1960s and 1970s. Counselor skill training (see Carkhuff 1969, 1971, 1972) attempted to enhance such qualitative dimensions of counseling as empathy and genuineness. Early studies concentrated on skill acquisition and were designed to determine whether counselors could acquire and be assessed on these qualitative counseling skills. The next research step was to assess the question of skill application: Did trainees apply their newly acquired skills in a real counseling situation? Studies of skill application led naturally to studies of benefit. If counselors used these skills in counseling, what benefits accrued to the counselor and client? Concurrent with research on acquisition, application, and benefit, work was also being done on the reliability and validity of the instruments used to measure the effectiveness of counselor skill training. Assessments using simulation and role play techniques were found to possess predictive and criterion validity.

Client skill training research seems to be following a similar path. While the three major lines of research—acquisition, application, and benefit—can be carried out concurrently, there is an underlying developmental theme to the research process. Investigations of skill acquisition (training process) ask: Can severely disabled psychiatric clients learn skills and, if so, what is the best way to teach these skills? With this line of research underway, researchers can begin to address the question of skill application (generalization): Can clients apply their acquired skills in the environment of need? A corollary question concerns the issue of benefit: If clients do in fact apply these skills, what benefits do they receive? Throughout these three overlapping phases of research, questions concerning the reliability and validity of the assessment instruments are continuously addressed.

In skill training research currently, application and benefit studies lag behind acquisition studies. Yet, the demonstration of generalization is clearly the paramount issue confronting skill training researchers. Ultimately, it is to be hoped that a comprehensive outcome evaluation strategy will become a reality in this field, and that investigators will describe the skill training process along the dimensions of client understanding and involvement; client skill acquisition; client application of skills in the appropriate environment; client benefits accruing from skill application; and reliability and validity of the assessment instruments used. Such a comprehensive research project will obviously be challenging to plan and implement.

With respect to drug treatment, more difficult research questions about its overall effectiveness are being asked. Irrespective of drug treatment's ability to forestall relapse and reduce symptomatology, what are its other effects—both positive and negative? From a rehabilitation perspective, does drug treatment impede or enhance the attainment of other outcomes? Given the neurological risks of long-term maintenance medication, can other types of rehabilitation interventions bring about similar outcomes? The comprehensive rehabilitation outcome assessment model encourages researchers to pursue these larger questions.

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[4] There are instruments to measure the general intelligence quotient of the chronically disabled or the particular type of thought disorder interference present. Lacking, however, are instruments to assess those client physical or emotional skill components necessary for the disabled to learn, or the ability to apply such skills in a learning environment.

Lastly, a comprehensive outcome model can help community support program researchers progress beyond the question that has thus far preoccupied them: Has the number of days the client resides outside the hospital been increased? Other questions are also relevant. When clients reside in a supporting community setting, does their ability to function improve? If their abilities and skills have not improved, then their benefits will probably also disappear if and when the support system is withdrawn. If this is so, then how can a support system and a skill training intervention be successfully integrated so as to maximize the rehabilitation outcome? No matter what the research design, a comprehensive outcome assessment model can help investigators in their attempts to understand how a supportive type of intervention does and does not affect client skills and benefits.

Summary

No matter which type of rehabilitation intervention is researched, the use of a comprehensive outcome planning model can serve to qualify the sometimes unbridled enthusiasm which accompanies any innovative treatment strategy. Using tables 1–5 as a guide, a researcher can systematically plan, during the research design process, exactly what process and outcome criteria will be assessed. This planning will facilitate a more comprehensive and programmatic attempt at rehabilitation research. In this way, comparisons between studies can be facilitated, consistent distinctions can be made between process and outcome measures, inferences derived from the research data can be correctly limited, and the researcher can be encouraged to examine his data for intended and unintended effects (positive and negative) of a rehabilitation intervention. Although the present review has focused on measures of client outcome, other measures such as family burden and cost of treatment are also important. However, positive changes in the client's world are the preeminent focus of rehabilitation. If psychiatric rehabilitation is to become a still more credible, viable treatment alternative, it must continue to direct its efforts toward answering the question: What's in it for the client?

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Assessment of Outcomes in Community Support Systems: Results, Problems, and Limitations

by Leona L. Bachrach

Abstract

Assessment of outcomes in community support systems for chronic mental patients is associated with a number of difficulties, including the lack of an operational definition, the need to study synthesized programs as approximations to organic community support systems, and severe methodological deficits within existing studies and in cross-study comparability. Although outcome studies indicate that community support programs show some apparent advantages in the treatment of patients, treatment gains are limited and tenuous. Moreover, interpretation of study results must be tentative because of methodological and programmatic limitations. Improved program evaluation and impact evaluation procedures are necessary to assess the efficacy of community support systems both in enhancing patient care and in providing solutions for the problems associated with deinstitutionalization.

In 1971, the National Institute of Mental Health (NIMH) sponsored a conference on mental health planning and community organization at the University of Missouri. The proceedings of that conference were published in a good-sized volume and then, like the proceedings of many conferences, consigned to a shelf. Recently I came across those proceedings and discovered, buried in the appendices, a paper that discusses the objectives and functions of outcome assessment in community-based mental health services (Stumpf 1973). Several purposes of outcome assessment are developed, and these may be paraphrased as follows: adding generally to the field of knowledge concerning an intervention or treatment approach; evaluating the degree to which the objectives of a given program using that intervention are being accomplished; re-evaluating the validity of the objectives of the intervention; and providing feedback, through the recycling of information, to initiate systems modifications.

The first of these purposes of outcome assessment is to broaden the base of knowledge. The second purpose, assessing a particular program's outcomes and their implications, falls within the purview of traditional program evaluation. Schulberg (1977) refers to this function as the "assessment of performance." It inquires into what tangible outcomes may be attributed to a given program's efforts by measuring the effects of specific actions in that program on a finite target population.

The last two purposes of outcome assessment, re-evaluating the validity of objectives and providing feedback for systems change, are related to what Schulberg (1977) calls "the assessment of adequacy." They deal with the extent to which a specific program contributes to the solution of a community's problems and thus view program outcomes from a global perspective. This approach has been referred to elsewhere as "impact evaluation" (Bachrach 1980*b*) in order to differentiate it from more traditional program evaluation techniques.

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The present article departs from this conceptualization of the functions of outcome research. It will discuss the major findings of systematic studies in a variety of community-based programs, the methodological difficulties limiting those studies, and the more global systems implications of community support interventions. The target population consists of persons with chronic mental disorders—particularly those diagnosed as schizophrenic—who have illnesses of such persistence and severity that, without special supports, they are "unable to maintain a stable adjustment to community life" (Test and Stein 1978, p. 351).

Background

Two recent overview articles, one by Test and Stein (1978) and one by Braun et al. (1981), intensively analyze the existing literature on community support programs. Each overview summarizes the results of some 30 controlled studies. The exact number of programs involved depends on how many times one counts a specific program that has been modified and restudied. Both of these articles describe and distill the research results in a narrative format. The piece by Braun and his colleagues also provides, in tabular form, precise comparisons of such details as study design, sample size, diagnostic and demographic characteristics of study group, control situation (e.g., long- vs. short-term hospitalization), specific outcomes assessed, and duration of study period.

These two overviews are so thorough and insightful that I shall make no further attempt to analyze individual community support programs. Anyone wishing to review the outcomes of a particular experimental effort is referred to these excellent summary articles. Instead, I shall use these articles, as well as other relevant literature, as the basis for a more consolidated analysis of the outcome research and its implications.

The internal validity of outcome studies in community support programs—i.e., whether the conclusions presented flow logically from the data collected—is highly variable. Some of the studies are quite meticulous in their methodologies, have excellent designs, and avoid unwarranted conclusions. Other studies vary in their methodological adequacy and often present results that are difficult to confirm.

Much more serious, however, is the fact that the research shows relatively little cross-study comparability. Although individual studies may be credible, the corpus of research has extremely limited generalizability. The result is that, while considerable effort has been expended on the systematic study of community support interventions, very little evidence can be adduced concerning the efficacy of the sum of these interventions. There are two major reasons for these restrictions on generalizability. One is conceptual and definitional: We do not as yet have a clear delineation of what community support systems are and so must approach the task of evaluating them inferentially. Secondly, differences in study design and populations assessed in the existing research, as well as methodological weaknesses in individual studies, make it very difficult to compare results and to generalize across studies.

Nonetheless, some limited generalizations can be made. Before I present these results and evaluate them, however, I should like first to discuss the conceptual difficulties inherent in attempting to study outcomes in community support systems.

Characterizing a Community Support System

The term community support system has been variously defined (Task Panel 1978). With specific reference to chronic mental patients, the definition most widely used for program planning purposes is that proposed by NIMH. That definition and its implications are discussed in an article by Turner and Shifren (1979).

According to the NIMH conceptualization, a community support system for the chronically mentally ill is a "network of caring and responsible people committed to assisting a vulnerable population to meet their needs and develop their potentials without being unnecessarily isolated or excluded from the community" (Turner and Shifren 1979, p. 2). In an attempt to standardize this definition NIMH has described 10 basic criteria for identifying community support systems for this population.

Such a system must, first, have a mechanism for identifying persons in need and the ability to "reach out to offer appropriate services to those willing to participate" (Turner and Shifren 1979, p. 3). It must, second, offer patients assistance in applying for and obtaining such entitlements as disability income and other benefits. Third, it must offer 24-hour crisis assistance in "the least restrictive setting possible" (Turner and Shifren 1979, p. 4) (although restrictiveness is not precisely defined). Fourth, it must provide psychosocial rehabilitation services for the target population. Fifth, services must have indefinite duration and potentially be available for individual patients' lives.

Sixth, the system must provide adequate medical and mental health care for patients. Seventh, it must include backup support for family, friends, and community members in order to minimize the burden imposed by the long-term care of chronically disabled individuals. Eighth, the system must engage and involve concerned community members in such a way as to maximize the contribution of natural helping networks, self-help groups, and voluntary community organizations in caring for the target population. Ninth, the system must operate so as to protect patients' rights and ensure that their civil liberties are not denied them. And, finally, the system must provide for the binding, integration, and coordination of all services needed for any particular patient, a function described as case management (Turner and Shifren 1979).

In the NIMH conceptualization, community support systems represent a "response to the progressive nuclearization of the family and are intended to provide the support that has been lost because of the dissolution of extended kinship networks or discharge from the hospital" (Mosher and Keith 1980, p. 35). They serve as antidotes to the frequently observed fact that persons suffering from chronic mental disorders are apt to be characterized by a high degree of social isolation (Beels 1978; Cohen and Sokolovsky 1978; Hammer, Makiesky-Barrow, and Gutwirth 1978; Beels 1979; Sokolovsky et al. 1978; Lamb 1979).

Thus, community support systems offer a basic response to the problem of providing for chronic mental patients both the nuclear and extended family relationships that are so often missing from their lives and whose restoration is considered to be a necessary element in their care. These programs are designed not only to furnish for patients those benefits that Budson (1978) perceives as the primary functions of the nuclear family—the socialization and maintenance of individuals—but they also strive, by providing the means and motivation for patients to participate in society, to afford these individuals the *gemeinschaft* life experiences and extended kinship supports that are identified as the essence of social networks (Pattison et al. 1975, 1978; Budson and Jolley 1978; Garrison 1978; Task Panel 1978; Beels 1979; Froland et al. 1979).

Definitional Difficulties

Now, this description of community support systems, while comprehensive and detailed, lacks the specificity of an operational definition. It cannot, as it stands, be used to locate existing community support systems. What standards shall we use for ascertaining a given program's validity as a "true" community support system? How much of each of the 10 criteria is needed for a particular effort to qualify? Must all 10 criteria be present, or only some of them, and in what mix? If resources are limited, who, among the most seriously ill, must be served? Must a given program serve all persons with chronic mental disorders who live within a defined geographic area, or only some of them, and, if only some, which ones? These are only a few of the many questions that are unanswered by the existing definition.

Although the difficulties associated with confirming the existence of community support systems with this definition are sufficient for us to conclude that we cannot know whether such programs actually exist, the literature contains descriptions of a number of programs that appear to qualify. Such efforts include the very noteworthy Fountain House program in New York City (Beard 1978; Beard, Malamud, and Rossman 1978); the Training for Community Living program in Madison, Wisconsin (Test and Stein 1976; Stein and Test 1979); the Southwest Denver community mental health program (Polak and Kirby 1976; Polak 1978); the Places for People program in St. Louis, Missouri (Anonymous 1976; Sandall, Hawley, and Gordon 1975); and the Sacramento County (California) mental health system (Barter 1975; Sacramento County 1977; Barter 1978; Langsley, Barter, and Yarvis 1978; Langsley and Yarvis 1978). It must, however, be emphasized that these various programs cannot be readily established as "true" community support systems—not because of any inherent lack in the programs themselves, but rather because the criteria for identifying them as community support systems lack specificity.

The question of whether community support systems exist except as an ideal concept notwithstanding, it is my strong feeling that localized initiatives that reflect the sense of the NIMH conceptualization, even if they depart from the literal description in some particulars, do in fact exist and that they are not at all limited to the well-known programs just enumerated. I have heard numerous such programs enthusiastically described at conferences in a variety of "show-and-tell" presentations.

Even more importantly, the existence of programs that fulfill the substance of the NIMH criteria makes sense intuitively. One might go so far as to guess that these kinds of programs exist wherever chronic mental patients are successfully and humanely served, whether in the community or in a hospital setting. This generalization makes sense not only because of what we know about the needs of persons with chronic mental disorders but also because of what is more generally known about human behavior (Task Panel 1978). An eloquent statement by Stein (1979, p. vii) conveys the rationalization that underlies this argument in its position that chronic mental patients are "no different from the rest of us in needing a [social] support network to maintain themselves in their environment. Unfortunately, however, their emotional disabilities are so serious and persistent that, without special help, they are unable to develop and maintain such a network." As a result, Stein maintains, long-term psychiatric patients generally do poorly when they live in the community without the benefit of specially developed supports.

But it is a long way from intuition to scientific assessment, and the argument that community support systems exist because effective treatment cannot take place in community settings without them is circular. More specific knowledge is needed.

Since we lack objective means for reaching consensus as to what constitutes a "true" community support system, we cannot approach the task of assessing outcomes directly but must instead contrive to do so inferentially. Moreover, assessment of community support system outcomes can only be performed if the programs that we study are themselves organized and conducted according to experimental design. They must, in short, be *bona fide* research efforts that allow for the objective assessment of outcome.

There is, in fact, a class of planned community-based programs for chronic mental patients that fulfills both of these criteria. Referred to by Braun et al. (1981, p. 736) as "experimental alternatives to hospital care," these programs, according to reports of their operation, appear to be in accord with the NIMH criteria for community support systems. Moreover, they serve as the foci of research efforts that are documented in such a way as to make objective evaluation feasible.

These experimental alternatives to hospital care generally follow one of two formats. Either they exist as alternatives to mental hospital admission—i.e., they take the place of, and serve in lieu of, placement on hospital rolls; or they exist as "aftercare" programs for patients already hospitalized. In some instances these aftercare programs are planned—in accord with the concept of continuity of care (Bacharch 1981)—as community-based extensions of care after a patient's hospital stay has been concluded. In other instances, the patient is deliberately released to the community before his hospital treatment is deemed completed, because the community alternative is in place and is believed to be—in line with the doctrine of the least restrictive alternative (Bachrach 1980*a*)—a better place for him to reside.

Organic vs. Synthesized Community Support Systems

It cannot be emphasized too strongly that assessment of outcomes in these community-based experimental alternatives to hospitalization is *not* the same thing as assessment of outcomes in *bona fide* community support systems. The former merely approximate the latter. Because these are two separate entities, I should like, for purposes of this discussion, to distinguish between "organic" and "synthesized" community support systems.

Organic community support systems emerge as answers to a community's perceived needs and are highly idiosyncratic responses to local problems. Every organic community support system is a unique entity because it reflects the problems and the culture of the community in which it is found. Typical of these enterprises are the Open Door in Barrington, Rhode Island (Carroll 1980); the Way Station in Frederick, Maryland (Mortensen 1980); 62 Barre Street in Montpelier, Vermont (Washington County 1980); Mountainhouse in Asheville, North Carolina (Anonymous, undated); St. Luke's House in Montgomery County, Maryland (Dearden and Petersen 1980); the Day Treatment Program in Angelina County, Texas (Anonymous 1979*a*); Cedar House in Oneida, New York (Straussman 1980); and Westside Lodge in San Francisco (Harris 1979).

My impression, based primarily on oral descriptions of these programs but reinforced by a number of site visits and occasional pamphlets, flyers, and articles, is that they are generally located in communities where resources are so scarce that residents have little choice but to deal directly with deinstitutionalized patients. Often, though not necessarily, these are rural or isolated communities where the chronically ill are highly visible, and there is little in the way of woodwork into which they can fade (Bachrach, in press). The use of social pressures to encourage civic and church groups to join in the support effort is not at all rare in these programs.

Organic community support systems may occur as "response[s] of the private sector to failures of the medical and social welfare systems to provide adequately for the needs of patients" (Mosher and Keith 1980, p. 35). Or they may operate with partial or total state and/or local government backing. Not infrequently, they combine the sum of public and private resources available in a given area. Indeed, these programs are generally characterized by a pragmatism so fundamental that funding structures are quite unpredictable. Money is taken from wherever it can be obtained, even if the amount is small and the duration of the financing is uncertain. Sometimes a local "angel" funnels resources into the program, and, when this occurs, it provides encouragement to the staff and reinforces the generally positive psychological milieu that seems to be a hallmark of these programs. Indeed, an optimistic outlook tends to persist in organic community support systems in spite of constant preoccupation with the program's survival.

Personnel in organic community support systems generally take great pride in their efforts and exhibit a deep concern for patients' needs. Goals tend to be expressed in terms of patients' overall welfare rather than measurable outcomes. It is not surprising that these programs typically lack an experimental approach. Workers tend to be more concerned with the day-to-day problems of service provision and with the effort of assuring program survival than with testing hypotheses about treatment interventions.

Organic community support systems, in sum, represent the means that some local communities have developed for coping with their own deinstitutionalization needs.

I recognize that in this conceptualization I have perhaps idealized organic community support systems as pristine, patient-oriented entities that are unencumbered by territorial disputes and bureaucratic demands. If this description is a bit idealistic, however, it still has the virtue of serving as an ideal type against which to measure synthesized community support systems—i.e., the experimental alternatives to hospitalization that serve as approximations to these organic community support systems.

Synthesized community support systems have neither the spontaneity nor the uncertainty of the programs that they simulate. They are interventions planned to test hypotheses, to elaborate on the conditions under which selected variables have specific outcomes. By contrast, organic community support systems are relatively spontaneous and free of the effects imposed by artificial experimental conditions and the categorical personnel and service requirements that frequently accompany them. This does not, of course, mean that the synthesized programs are poor ones, and my differentiating them from their organic counterparts is in no sense pejorative. Quite to the contrary, many synthesized community support systems are widely perceived as highly commendable and desirable alternatives to hospital placement in those communities where they exist (Stein and Test 1978; Talbott 1981). A number of these programs originally started out as organic programs and only later, after they were recognized as having special value in the delivery of services to chronic mental patients, were given supplemental funding earmarked for research purposes.

It should be noted that, in actual operation, both organic and synthesized community support systems usually limit their enrollment in some way. With finite resources available to a given program, some method of assigning priorities, either explicit or subtle, is generally used. Some programs disallow patients with a particular problem in living, such as substance abuse or severe acting out behavior, and these patients are systematically eliminated because of their potentially deleterious effects within the program's milieu or on community relations. Other patients may be excluded from the synthesized programs because they do not fit the requirements of the experimental design.

Research Findings

In the absence of research findings on organic community support systems, it is possible to look instead at those from synthesized programs. The major substantive findings on outcomes in these latter programs, as summarized in the Test and Stein overview, are as follows:

1. Community-based programs that have been planned as alternatives to hospital admission for the care of persons suffering from chronic mental disorders can, in fact, serve that purpose effectively. Given programs that are directed toward individual patient care (as opposed to dumping), it is altogether possible to substitute community-based efforts for hospital care with results that are not worse than hospital care and are generally beneficial to the patients enrolled in them. Community-based programs that show positive results are typically characterized by high staff-to-patient ratios and appear to benefit from funding patterns that assure, at least for the duration of the study, their optimal and continuing operation.

It may be noted that the actual number of experimental programs planned as alternatives to hospital admission, as reported in the literature, is quite small. Test and Stein, who include certain nonresidential day hospital programs in this category, count a total of 10 experimental alternative to hospital admission programs; while Braun et al., who exclude day hospitals, count only seven.

2. Most synthesized community support systems, instead of serving as alternatives to hospital admission, exist as experimental substitutes for traditional hospital care, specifically as aftercare efforts for patients previously hospitalized. These programs also appear to achieve generally favorable results but only so long as they are characterized by individual programming, adequate financing, and favorable staff-to-patient ratios. Experimental evidence supports the view that synthesized community support systems can be instrumental in substantially reducing rehospitalization rates for patients. However, while these programs are generally known to reduce readmissions, they do not altogether prevent them. Even where aftercare is provided, large numbers of patients drop out of treatment, and these individuals frequently return to hospitals.

3. There are relatively few differences reported in the symptom levels of chronic mental patients treated in experimental synthesized community support systems and in in-hospital control programs. In both kinds of settings, the "usual course" is an "early reduction in symptomatology" followed by a "levelling off as long as persons remain in treatment" (Test and Stein 1978, p. 360).

4. Research conducted to date is inconclusive as to whether care in synthesized community support systems results in improved psychosocial functioning among chronic mental patients. A number of individual studies reveal no significant differences in psychosocial functioning as between patients enrolled in hospitals and those who are cared for in community settings. However, the literature does suggest that, in those community-based programs that include a "very intensive intervention targeted specifically toward the psychosocial area" (Test and Stein 1978, p. 360), distinctly positive outcomes are discernible. Test and Stein (1978, p. 360) thus conclude that "modest gains in psychosocial functioning in the community can be achieved . . . through direct and intensive intervention in specific activities of daily living in the community with gains being sustained as long as treatment lasts," and there is a strong implication that direct interventions must be aggressively pursued if the advantage is to continue.

It may be noted parenthetically that a major benefit of providing social skills training in synthesized community support systems is their *in situ* advantage. There is general agreement that accomplishments gained in environments other than those where patients will ultimately reside are inadequately generalized to "real life" situations (Wallace et al. 1980). Accordingly, if patients are to be discharged to the community, training for community living is most appropriately conducted after hospital release.

5. Consumer satisfaction with treatment appears to be greater among patients cared for in synthesized community support systems than among those placed in hospitals.

Although some studies of individual programs claim a variety of successful outcomes beyond these several general results, the points just enumerated appear to constitute the bulk of generalizable outcomes in the various synthesized community support systems studied by Test and Stein (1978), and the conclusions of Braun et al. (1981) essentially concur. Braun et al. conclude their review of substantive findings with the observation that "selected patients managed outside the hospital in experimental programs do no worse than and by some criteria have psychiatric outcomes superior to those of hospitalized control patients" (p. 747). These authors do note, however, that where differences between the two groups are observed, they tend for the most part "to favor the experimental group, particularly with respect to hospital readmissions and, in a number of instances, with respect to independent functioning" (p. 747).

Methodological Problems

It must be noted that even these modest outcomes attributed to synthesized community support systems in the two overview articles do not exist in a vacuum. These outcomes should be perceived as effects only partially attributable to support system milieus because of the simultaneous operation of numerous other variables such as drug treatment, talking therapies, patients' demographic characteristics and institutional histories, and the like (Bland and Orn 1977; Strauss and Carpenter 1977). Because of such difficulties, Mosher and Keith (1980) contend that research into the outcomes of community care for chronic mental patients is "flawed." A number of critiques, less comprehensive in scope than the two overview articles, but productive of penetrating analyses of the state of the art, accordingly echo the tentativeness and caution expressed by Test and Stein (1978) and by Braun et al. (1981).

A first source of methodological concern revolves around the absence of clearly stated program goals. Existing studies generally fail to specify the goals of the programs whose outcomes they are assessing, and this failure makes it difficult to assess the degree of fit between the program's philosophy and its outcomes (Bachrach 1974). The failure to specify program goals in research reflects a more generalized failure to be specific about the goals of the programs themselves.

The importance of precision in goal setting for program planning is discussed in a report on California's mental health system (Teknekron 1977) that isolates several desiderata in service planning, such as having patients reside in the community, minimizing hospitalization, maximizing patients' independence, and curing, or eliminating, mental illness. If the first two of these goals, living in the community and minimizing hospitalization, are basic to a program's aims, the patient's mere presence in the community provides sufficient evidence of a successful outcome. But if the last two of these goals, maximizing independence and eliminating mental illness—goals about which some investigators are quite pessimistic (Lamb 1981; Zusman and Lamb 1977; Hansell 1978)—are to be pursued, the evaluation of outcomes becomes infinitely more complicated.

Thus, the absence of explicitly stated program goals, a serious methodological problem, more basically represents a major flaw in program design, one that reveals a fundamental lack of direction that very likely interferes with the provision of services. In this instance, methodological and service delivery deficits appear to be linked.

In the absence of clearly stated program goals, it is not unexpected that a second major source of methodological concern about the assessment of outcomes in synthesized community support systems is the general absence of adequate indices of outcome. The most widespread outcome measure used in studies of community support interventions is recidivism or rehospitalization.

Anthony, Cohen, and Vitalo (1978) support the use of recidivism as an outcome measure, not only because this criterion provides a data link to previous studies, but also because it is easily standardized, has face validity as a measure of program success, and has traditionally served as a standard for program planning and development. An early study by Lehrman (1960) concurs in this judgment.

These advantages notwithstanding, a number of authors have questioned the preponderant use of recidivism as an index of program success (Rosenblatt and Mayer 1974*b*; Bachrach 1976*b*; Strauss and Carpenter 1977; Stein and Test 1978; Smith and Smith 1979; Mosher and Keith 1980; Braun et al. 1981). Taube (1974) demonstrates that rehospitalization may be an artifact of the institutional history of a given program's patient population. Aggregate readmission statistics for a program reflect the number of people at risk for rehospitalization. And, since number of prior hospitalizations is one of the best predictors of recidivism (Weinstein, DiPasquale, and Winsor 1973), a program's success in keeping patients out of the hospital will be affected by the degree to which its enrollment is weighted with multiply hospitalized individuals.

Recidivism is also known to be a correlate of a variety of other variables, such as length of hospital stay, administrative policies concerning readmission, out-of-hospital living arrangements available to the patient, and emotional climate within the patient's family (Buell and Anthony 1975; Rosenblatt and Mayer 1973; Weinstein, DiPasquale, and Winsor 1973; Rosenblatt and Mayer 1974*b*). Relying on recidivism as the major outcome variable in community support programs is thus, at best, a questionable practice.

Once again, there is a parallel for this methodological deficit in the area of service delivery. In the absence of adequate outcome indices, a program that relies on rehospitalization rates to measure success may easily make community tenure its major *de facto* goal.

Third, when outcome measures other than recidivism are used in studies of synthesized community support systems, their adequacy is not clearly established (Gottesfeld 1976; Test and Stein 1978; Braff and Lefkowitz 1979; Docherty et al. 1980). This situation is hardly surprising. In the absence of explicit goals, even accepted instruments will produce results whose meaning is difficult to assess.

Outcome criteria used in studies of community support programs are numerous, diverse, and largely unstandardized and include such specific events as psychiatric symptomatology; psychosocial functioning as measured by residential stability, social autonomy, role performance, employment, social functioning, and the like; and patient satisfaction. Of these measures the most valid instruments, according to Test and Stein (1978), are those that deal with symptomatology. Other instruments currently used are something less than satisfactory, according to these investigators, and the "major need in standardizing research in community treatment is the development of a sensitive instrument to measure community adjustment" (p. 361).

In short, if effective outcome research is to be performed, it is necessary not only to state program goals with exactness but also to take care to use measures that reflect progress in the attainment of those particular goals. Once again, the failure to do so in studies of synthesized community support systems reflects potential program deficits and says, in effect, that caregivers have not developed effective ways of telling whether their interventions make any difference.

A fourth difficulty attending the measurement of outcomes in synthesized community support systems derives, as suggested earlier, from the absence of methodologies to assess the interactive effects of patient care techniques. Since outcome research in community-based mental health efforts generally suffers from the existence of "multiple interventions, either concurrent or sequential" (Klein 1980, p. 122), it is necessary to use measures and statistical techniques that permit us to extract from a complex field of variables the precise ways in which specific interventions or treatments affect patient status. It is also important to know something about the combined effects of interventions (Carpenter 1979). This, after all, is what outcome research is all about.

One specific and very troublesome area of concern is the confounding nature of drug treatments. It is suggested by a number of investigators (Braun et al. 1981; Goldberg 1980; Rose 1979; Schooler 1980; Schulz 1980) that drugs may account for a substantial portion of the apparent success of synthesized community support systems in the treatment of chronic mental patients. To control for this and other interactive effects, it is necessary to have what Coulton and Solomon (1977) refer to as "rigorous research design" that "allows an investigator to know, with a stated degree of certainty, that changes in the dependent variable are due to changes in the independent variable" (p. 4). Without this, we have only "very partial answers" (Klein 1980, p. 122) to specific questions concerning outcomes.

Fifth, it is difficult to assess the outcomes of synthesized community support systems because study groups tend to be inadequately standardized with respect to their diagnoses, degree of psychopathology, symptomatology, institutional history, and other patient characteristics (Goldberg 1980; Gottesfeld 1976; Carpenter 1978). When patients with a wide range of characteristics are thus indiscriminately used in the conduct of research, comparability of results across studies is hard to achieve, and it is very difficult to "resolve contradictory findings and identify those patient characteristics that may predict responsiveness to treatment" (Wallace et al. 1980, p. 58).

Variation in level of premorbid adjustment appears to be a particularly serious confounding variable. In evaluating a publicly funded psychosocial rehabilitation program in Orange County, California, Auerbach and Pattison (1976) conclude that there are basic population differences among the chronically mentally disabled that must be considered in planning community support services. Auerbach and Pattison (1976, p. 39) distinguish between two groups of patients: those who have at some time "achieved some degree of social competence and ability to function in community life" and thus have "some repertoire of personal and social resources" to aid in their rehabilitation; and those "silent disabled" who have "led marginal styles of social existence . . . [and] have not acquired effective levels of social competence in the past, nor developed social resources as part of their support system of life." These investigators suggest that it is extremely important to specify patient subgroups in planning community support programs, and they call for interventions that are "socially compatible with the life experience and life style" of different patient populations.

I refer to these observations by Auerbach and Pattison because their argument is presented so cogently. Even though they draw their conclusions from studying a program with an extremely heterogeneous target population (enrollees include mentally handicapped public assistance recipients with both psychotic and nonpsychotic diagnoses), the problem they discuss is present even within an exclusively psychotic patient population, which itself tends to be quite heterogeneous in functional level, symptom level, and rehabilitative potential (Lamb 1981). Rabkin (1980), for example, discusses widespread variations in level of premorbid adjustment even among patients diagnosed exclusively as schizophrenic.

Since patients vary so widely in their history of coping with social and occupational situations, it is reasonable to expect outcome studies to control for patient characteristic variables. But assessments of outcome in synthesized community support systems widely fail to take this confounding factor into consideration, and both intra- and interstudy comparisons in outcomes are rendered extraordinarily difficult.

Finally, the variable of time is subtly associated with a variety of problems in assessing outcomes in synthesized community support systems. Carpenter (1979) suggests that, ideally, data should be gathered at four different times in outcome studies: at a point preceding the treatment intervention, at the beginning of the treatment period, at the conclusion of the treatment period, and at some followup date after the treatment period. But this kind of systematic study is rare in outcome assessments of community support programs.

Even when attempts have been made in individual studies to collect longitudinally valid data, there is so little uniformity across studies that generalizability is severely limited (Bachrach 1976*b*). Results of interventions in these studies are assessed variously at time intervals ranging from several months to 5 years (Braun et al. 1981). The problem goes beyond the need to allow sufficient time for interventions to have their desired effects, a situation that concerns some investigators (Mosher and Keith 1980). It extends to the need for consensus about what to expect from programmatic interventions and reflects a widespread and basic uncertainty about when to begin to look for effects.

In summary, the study of outcomes in synthesized community support systems is limited by an array of methodological difficulties, including the absence of clearly defined program goals, reliance on recidivism as the major outcome measure, use of other outcome measures whose validity has not been established, the absence of methodologies sufficiently sophisticated to account for interactive effects, the lack of standardization in study groups, and the failure to ground research with "an appropriate definition of the time frame" (Schooler 1980, p. 133) in which effects may be sought.

The most important thing about these methodological deficits is that they represent something more than limitations in research design. I have pointed out a number of instances in which they also reflect basic uncertainties in the art and science of delivering community-based services to patients with chronic mental disorders. Fuzziness in program design and program direction begets fuzziness in investigation. The methodological shortcomings discussed here are thus, in the most basic sense, program shortcomings. Failures in setting goals, defining outcome criteria, controlling for interactive effects, and making judgments about the time in which those effects should become apparent are as much deficits in program design as in methodology. And deficits in program design ultimately tend to affect patient care.

Therefore, I would supplement the reports of qualified success in synthesized community support systems with the somewhat more cynical view that what looks like success may, unfortunately, be no more than a reflection of the hopes and ego involvements of the programs' investigators (who also are often the programs' caregivers and administrators). The most certain conclusion we can draw from the data reported so far is that we do not really know very much about outcomes in these programs beyond the fact that, given adequate service structures and resources, they are not harmful to patients. Assessment of outcomes in these programs is premature and is too frequently biased in a number of ways. These interventions may be very good for their respective target populations. Or they may be of little consequence, even though our intuitions tell us that this is unlikely.

For more detailed assessments to be conducted, there must be both improved methodologies and better-integrated program designs. At present, we know neither what to look for nor how to look for it in our efforts to assess program success.

Impact of Synthesized Community Support Systems

I should like now to shift the focus of this article, in keeping with the purposes of outcome assessment as detailed in the introduction, and examine outcome research in synthesized community support systems from a totally different point of view. Since outcome assessment is relative to program objectives, it behooves us to ask what the general objectives of these programs are.

Although we have seen that specific patient care goals tend to be inadequately delineated in these synthesized community support efforts, there is far more certainty about broad program objectives. A review of the literature reveals the existence of two closely related, though distinguishable, kinds of program ends. One set of objectives is patient-oriented and is concerned with improving direct patient care. The second is systems-oriented and is related to enhancing the humanitarian goals of the deinstitutionalization movement—namely, reversing those dehumanizing influences that are generally thought to be part and parcel of institutional care (Bachrach and Lamb, in press). A major clue to the importance of this second class of objectives is provided in the statement by Schulberg (1979, p. 1433) that NIMH's recent community support initiative is "being heralded by some as the solution to the ills of deinstitutionalization."

The rationale for conducting outcome research in synthesized community support systems parallels these two kinds of program objectives. Individual controlled studies covered in the two overview articles represent attempts at traditional program evaluation, as described in the literature of that field (Zusman and Ross 1969; Markson 1975; Arthur D. Little 1976), with the express purpose of testing specific patient care techniques. Beyond this evaluative purpose, there is a second manifest reason for studying synthesized community support systems. It is thought that the study of these programs will elucidate problems associated with community-based treatment for the target population and that the knowledge derived can then be used to plan program strategies—in short, to provide feedback for improving the community-based system of care (Schulberg 1979).

It is possible that the first of these two outcome study objectives can some day be accomplished—that methodological deficits can be contained in such a way that controlled studies of synthesized community support systems will eventually yield viable program evaluations. I would contend, however, that even if these studies were to be conducted rigorously, they still could not be used for the purpose of assessing the problems of deinstitutionalization. A wholly different kind of approach from that followed in traditional program evaluation is required to study solutions to the multitude of problems attending deinstitutionalization. What is needed is a framework that asks systems-relevant questions, one that permits the kind of impact evaluation that is necessary for effective policy formulation (Bachrach 1980*b*).

Impact evaluation is distinguished by the kinds of questions it poses. Instead of looking inward to the workings of individual programs as does traditional program evaluation, impact evaluation typically looks outward and asks, "So what?" It thereby focuses on the broader implications of programs for the delivery of services to the total population of persons with chronic mental disorders. By using events in the external world as yardsticks, impact evaluation possesses an element of reality testing that is of particular importance in service planning for chronic mental patients, in view of the fragmented nature of mental health systems and the undisciplined, and frequently discriminatory, manner in which programs are often developed (Bachrach 1976*a*; Barter 1980; Beck 1979; Bradley 1976; Cramer 1978; Hansell 1978; Karwan, LoCicero, and Rasul 1980; Kirk and Therrien 1975; Raffo and Brody 1980; Rose 1979; Scherl and Macht 1979; Talbott 1979; Tarail 1980; U.S. General Accounting Office 1976; Williams, Bellis, and Wellington 1980).

That traditional program evaluation and impact evaluation serve different ends and require different methodologies is illustrated in a recent U.S. General Accounting Office (1978) report on the Veterans Administration personal care home program. Program evaluations reveal that this model effort of foster care placements for chronic mental patients, which is now nearly 30 years old, is highly successful in meeting the personal care needs of its enrollees. But impact evaluation is necessary to tell us that many more patients qualify for care in these homes than are actually served there. With impact evaluation we know that qualified patients tend instead to be hospitalized for such systems reasons as insufficient funding, unavailability of enough suitable community-based facilities to meet demand, lack of adequate commitment to the program from the VA central office, and patient and/or family resistance to out-of-hospital placements.

Unless specific impact questions are asked, individual programs run the risk of going off into their own orbits with little meaning for the complex and diverse needs of the total population of chronically mentally ill persons. Preoccupation with traditional program evaluation is, in fact, potentially dangerous because it holds the possibility of deflecting our attention from the severe and often unremitting problems that have been widely identified as serious issues inhibiting successful deinstitutionalization programming (Bachrach 1976*a*; Bassuk and Gerson 1978; Group for the Advancement of Psychiatry 1978; Halpern et al. 1978; Scherl and Macht 1979). In this connection, I would agree strongly with the assertion by Braun et al. (1981, p. 748) that, "given the magnitude of the social policy change entailed by deinstitutionalization and the two decades that have elapsed since it was put into motion, it is astonishing that so little productive effort has been put into evaluating the effects of the policy."

Avoiding the tendency to concentrate on effects in isolated programs instead of total systems is, in fact, the basis of systems theory as described in a recent article in *Science* (Miser 1980). According to Miser (1980, p. 209) the basic tenet of systems theory is that any given system is "merely a subsystem in a larger system— indeed, one of ever widening congeries of systems." Thus, for example, "a regional blood-collection and -distribution system supports the hospitals of its region, which are part of the nation's health care system" (p. 209). Systems theory holds that "the purposes of the subsystems are subservient to the purposes of the larger systems of which they are parts" (Miser 1980, p. 209).

To paraphrase Miser, community support systems for the chronically mentally ill are subsystems within the mental health system which, in turn, is a subsystem that is partially within the general health care system and partially within the human services system. The purposes of community support efforts must in this sense be perceived as subservient to the purposes of deinstitutionalization, the major policy focus of the mental health system. If we wish to assess the outcomes of deinstitutionalization in order to change that policy and/or its implementation, we must look not to effects in isolated programs but rather to effects in the mental health system itself.

In this connection it is worth noting that experimental efforts necessarily differ from mental health systems in a number of critical ways. Mental health systems must serve all who are in need, not only persons who happen to fit in with some predetermined experimental criteria. Mental health systems must, in fact, serve even those who show little hope of improvement, although experimental programs may be very selective in their admission policies. Although experimental programs can, and in accord with their scientific aims should, focus their resources on a selected group of patients, mental health systems must deal with competition from different kinds of patients with a variety of disabilities. In short, experimental programs are generally too limited in concept to serve as testing grounds for the outcomes of deinstitutionalization.

Problems in Evaluating Deinstitutionalization

There is some reason to question whether it is even possible to assess the outcomes of deinstitutionalization because such an effort must necessarily entail tremendous complexities in both conceptualization and methodology (Bachrach and Lamb, in press). I would submit, however, that it is time to find out. We must attempt to supplement the traditional program evaluation efforts that are used for assessing outcomes in experimental programs with more extensive impact analyses. Although the need for impact evaluation has been known for some time, it is only recently that the literature has even begun to reflect the kinds of questions that need to be asked (Gaver 1976; Holder 1977; Stratas, Bernhardt, and Elwell 1977; Barter, McMahan, and Froland 1978; Boyd and Henderson 1978; James 1978; Bachrach 1979; Barrow, Gutwirth, and Schwartz 1979; Talbott 1979; Barter 1980; Stratas and Boyd 1981) and methodological approaches are still being developed.

I shall devote the remainder of this article to a discussion of several broad issues that are relevant to impact analysis in deinstitutionalization and that are essentially overlooked by the existing research into outcomes of synthesized community support systems. I have selected for this purpose four specific but interrelated areas of major systems concern in deinstitutionalization programming. These include inequitable priority setting within the mental health system; the failure to address the needs of all segments of the heterogeneous population of chronically mentally ill individuals; the limited relevance of a rehabilitation focus for all portions of the target population; and difficulties in placing certain kinds of patients within the mental health system.

Inequitable Priority Setting

If chronic mental patients are to be provided with adequate care, they must have access to the service system and its component parts. What this means, in effect, is that these patients must be acknowledged as the rightful recipients of whatever services the system has to offer. However, there is some evidence that chronic mental patients are discriminated against by the service system. In the community, for example, in lieu of adequate care they may be placed in residential facilities of questionable standards. They may, or may not, receive medication; and other forms of treatment are even more rare (President's Commission 1978).

That these conditions prevail is ironic. Originally, community mental health services were intended to eliminate the need for mental hospitals through the development of noninstitutional alternatives for the most seriously ill. Simultaneously, patients were to be released to the community, and the need for new admissions to these facilities was to be gradually eliminated: The nation would be served by a network of community mental health settings that would provide a wide variety of services for individuals with severe and persistent mental disabilities.

However, even though the "basic mission" of deinstitutionalization was originally to provide community-based treatment for the most seriously ill, "only limited aspects of the original conception have been implemented," and "the interest of most workers has gone off in other directions" (Zusman and Lamb 1977, p. 889). Community mental health today focuses largely on the treatment needs of the "healthy but unhappy," and the needs of the most seriously ill tend to be given low priority. Thus, Miller (1977, p. B1) writes of an "inverse system of care," in which "the most trained and skilled clinicians deal with the most articulate, interesting and likely to succeed clientele," while the existence of those patients most in need is largely ignored.

The net result of these inequities is discussed by Halpern et al. (1978) who describe the "irrelevance" of community care for the most disabled and draw the parallel that "expecting the chronically mentally ill patient to use the current mental health system is like expecting a paraplegic to use stairs. . . . The chronic long-term mentally ill person can't use the current mental health system because it's oriented toward people who have motivation, who have the capacity to develop insights, to change behaviors, to accommodate through socially acceptable behaviors" (p. 19)—characteristics not generally descriptive of persons with chronic mental impairments.

Nor is it realistic to think that these particular patients will themselves bear responsibility for initiating and perpetuating their own treatment in community settings. Persons suffering from chronic mental disorders very frequently are neither aggressive nor compliant (Amdur 1979; Barrow, Gutwirth, and Schwartz 1979; Braff and Lefkowitz 1979; Tessler and Mason 1979; Goldberg 1980). To the contrary, these patients tend to be singularly impotent when it comes to advocating on their own behalf. If they are not accorded top priority in the mental health system, they are unlikely to seek it for themselves. Their need for advocacy is basic.

Heterogeneous Target Population

Even when the most seriously ill have been acknowledged as rightful recipients of services, there has been a tendency to minimize the breadth of their needs in planning efforts. Goldman, Gattozzi, and Taube (1980) cautiously estimate that in 1977 about 900,000 chronically mentally ill individuals resided in institutions, including nursing homes, and an additional 800,000 to 1,500,000 resided in various community (i.e., noninstitutional) settings. Thus, a midpoint estimate in this range suggests that something over 2,000,000 persons with chronic mental disorders in a wide variety of demographic settings today require care.

Before the move toward community-based care, patients with these kinds of disorders generally entered state mental hospitals, where many remained for the rest of their lives. This essentially static population pool changed primarily as the result of new admissions and deaths, so that providing care was relatively simple. Virtually all services were given in a single physical setting, and the various services needed by the target population could, at least potentially, be readily effected.

Deinstitutionalization has, however, broadened the geographic base of the target population, so that the chronically mentally ill now possess a variety of institutional and demographic histories (Bachrach 1978). Part of the target population consists of hospital dischargees, and it is very difficult to deliver adequate services to two somewhat diametrically opposed subgroups of this population—those who are highly visible as they go again and again through the revolving doors of the service delivery system, and those who become virtually invisible (i.e., "fall through the cracks") as they exit from the doors of institutions and become, for all intents and purposes, lost to the service delivery system.

Although patients discharged from mental hospitals are most often associated with the term "deinstitutionalization," they in fact make up only a portion of the target population and are by no means the only chronically ill persons affected by the movement. Another group within the target population consists of never-hospitalized individuals who probably would have been institutionalized several decades ago and who, as the direct result of deinstitutionalization policies and practices, represent an ever-increasing percentage of the target population (Lamb and Goertzel 1977; Pepper et al. 1980). The medical, psychiatric, and social service needs of these individuals are very different from those of the ever-hospitalized.

Moreover, deinstitutionalization has also affected the provision of services for a number of patients who, despite deinstitutionalization efforts, continue to utilize state hospitals. These include the hospitals' "old long-stay," "new long-stay," and "short-stay" patients (Bachrach 1978; Shore and Shapiro 1979).

A study by Dorwart (1980, p. 338) at a state hospital in Massachusetts confirms that the residue of patients treated in hospitals today tends to have distinctive clinical and management needs that have been "accentuated by deinstitutionalization." These patients tend to exhibit acute psychotic symptoms, to be dangerous to themselves or others, to require intensive care, and to lack social skills. It is likely that the continuing diversion of resources toward the expansion and improvement of community-based services may work to the detriment of these patients, whose special needs require the financing of well-organized, well-staffed in-hospital programs (Ashbaugh and Bradley 1979).

All of these different groups of chronic mental patients should be regarded as the legitimate beneficiaries of planning efforts that are intended to improve patient care in this era of deinstitutionalization. At a time when financial constraints make it necessary to be as parsimonious as possible, we are thus faced with the task of arranging a multitude of services for a variety of patient populations in numerous settings. This is a systems problem of the first order and one that is not customarily considered in the evaluation of outcomes in synthesized community support systems. Because they are concerned with only a small portion of the target population of deinstitutionalization, these experimental programs fail to provide direction in planning services for the majority of persons with chronic mental disorders and thereby minimize the needs of that majority.

Limits of Rehabilitation

The Test and Stein (1978) overview reports that the modest gains in rehabilitation and psychosocial functioning made by some patients in experimental programs as the result of caregivers' very direct and continuing interventions are tenuous and will probably be sustained only so long as direct treatment continues. I believe that this rather discouraging finding is overshadowed by a situation that may appear to be even more pessimistic.

Within the target population of chronic mental patients there are individuals who are unlikely to show appreciable gains in skills accomplishments regardless of how direct and sustained the interventions may be (Abbott 1978; Hansell 1978; Lamb 1979; Stern and Minkoff 1979). These are patients who do not stand out as program "successes," and discussions of their needs are notable for their general absence from the literature. According to Lamb (1981), it is highly probable that for the majority of chronic mental patients rehabilitation, as measured by competitive employment, high levels of social functioning, and a general return to the mainstream of society, is simply not a realistic program goal. To the extent that these patients show any responsiveness to treatment at all, their achievements tend to be so imperceptible that they cannot be assessed by the conventional criteria employed for assessing outcomes in rehabilitation. Nonetheless, most synthesized community support systems continue to place heavy emphasis on rehabilitation, skills development, and the preparation of patients for activities of daily living; and such emphasis is considered to be essential, if not absolutely basic, to the development of community support systems (Turner and Shifren 1979).

This emphasis has the latent function of reinforcing the notion that all patients have equal rehabilitation potential, and caregivers are apt to behave as if this were the case. A recent study of admissions of chronic mental patients to a community-based facility in California, for example, reports that staff members frequently have difficulty in acknowledging the existence of patients whose rehabilitation potential is limited. This study asserts that staff predictions of patients' outcomes systematically exceed their ability to respond to treatment interventions—a situation that leads to caregivers' unwillingness to "accept the concept of limited goals" and to difficulties in caring for poor-prognosis patients (Solomon et al. 1980, p. 116).

Rossi (1978, p. 581) aptly points out that a delivery system "can simulate success by delivering treatments to individuals who are most likely to recover." Hence, so long as synthesized community support systems are designed to measure program success in rehabilitative terms, there is a serious risk of forgetting that it is sometimes necessary to measure success in some other way and that it is appropriate to use alternative goals for some patients. In fact, it is incumbent upon us to develop separate outcome measures for maintenance-level patients, measures that rely on other criteria—such as patients' responsiveness to environmental stimuli, or their personal comfort.

Unfortunately, however, the widespread emphasis on rehabilitation in synthesized community support systems predisposes us to place disproportionate emphasis on skills achievement, so that we tend to overlook alternative, but less dramatic, indices of humane and compassionate patient care in program planning.

Placement Difficulties

While some patients with chronic mental disorders are inappropriately placed in particular service facilities for political or financial reasons, or simply because appropriate community alternatives are not available to them (Sheehan and Craft 1975; Lund 1976; Booker 1977; St. Elizabeths 1977, 1979; Anonymous 1979*b*; Colen 1979; Faden and Goldman 1979; Fowler 1980), there are other patients for whom there appears to be no ready niche in a community-oriented system of care. This is an issue that has recently begun to surface in the literature, and it concerns patients whose needs are somehow anachronistic, or at least out of tune with current service delivery modes.

There are probably several varieties of these patients who "do not fit." Frequently, they are people whom Neill (1979, p. 209) describes as "blacklisted 'difficult' patients . . . whose presence engenders strong negative feelings" among treatment staff. Bean et al. (1979) refer to them more generally as "system misfits." Bassuk and Gerson (1980, p. 1513), who have encountered such patients in the psychiatric emergency ward of an urban general hospital, describe them as individuals "who, despite persistent efforts to engage them in ongoing treatment, keep returning to the emergency ward" where they comprise a familiar revolving-door population. Lamb (1980, p. 137) refers to these emergency service regulars as "psychiatric hoboes."

Closely related to, or part of, the problem of patients who do not fit in the service system are two other placement problems. One concerns patients whose preference and/or need for either long- or short-term hospitalization is not accommodated (Simon 1965; Spiegel and Keith-Spiegel 1969; Rosenblatt and Mayer 1974*a*; Colen 1977; Smith and Smith 1978). Subtle clues to the dimensions of this particular problem are provided in two studies of the reasons that former patients visit those wards in general hospitals where they were once hospitalized. Kramer and Rubinson (1978, p. 302) report that these visits frequently reflect either "meaningful relationships with staff members and other patients" or "continuing treatment needs of various kinds." Similarly, Gruber, Brown, and Mazcrol (1978, p. 734) write that visits by former patients represent a "response to real but unarticulated needs that are not being met by the mental health system" and that "while hospital readmission is commonly thought to indicate failure, it may be better to look on the brief hospital admission as an episode of temporarily increased dependency in the course of a long-continuing disability."

A second related problem involves the inappropriate placement of patients in the criminal justice system. Although Steadman and Ribner's (1980) study of criminal offenders in New York State concludes that deinstitutionalization practices and revisions in mental health commitment codes probably have not altered the composition of prison populations appreciably, Stelovich's (1979, p. 620) study in Massachusetts concludes that there is a "population of deinstitutionalized patients, who, lost to follow-up, [drift] into the legal system and [land] in prison." Whitmer's (1980) observations concur with the latter view.

In any case, a number of writers (Anonymous 1979*c*; Modlin 1979; U.S. General Accounting Office 1979; Anonymous 1980; Kaufman 1980; Nunes 1980) appear to agree that psychiatric services in prisons are generally less than optimal, and the implication is clear that at least some of the more seriously psychiatrically ill inmates would profit from more appropriate placement in service settings where the level of psychiatric care is consistent with their needs.

Robbins et al. (1978) assert that the number of patients who lack a place in the mental health system appears to be increasing as the result of deinstitutionalization practices. Yet, there is little in the literature on experimental community support programs that can shed light on this systems problem. Synthesized community support systems indeed appear to exhibit what almost amounts to a complacency in addressing placement questions. For the most part, each individual experimental program is described in the literature as if it represents one of two dichotomous choices, hospital care being the other. The notion of a range of placements for patients with a range of needs is very much played down in that literature.

Implications

The problems just discussed— inequitable priority setting, failure to address the entire target population, disproportionate emphasis on rehabilitation, and placement difficulties—may be seen as direct, if unanticipated, consequences of implementing deinstitutionalization policies and practices. Although they are by no means the only problems that attend deinstitutionalization, I think that they are particularly useful in illustrating the failure of synthesized community support interventions to deal with systems issues. They show that important conceptual work remains to be done in deinstitutionalization planning and that this cannot be accomplished by studying synthesized community support systems per se.

In the light of the serious problems that still surround deinstitutionalization, synthesized community support systems, unfortunately, may even appear to be guilty of oversights, irrelevancies, and deflections. This is, of course, an unfair indictment. Most of the caregivers and administrators associated with these programs are undoubtedly concerned with giving the best possible care to their patients and with testing the efficacy of their interventions in a scientific manner. They almost certainly have no grandiose wish to solve the problems of deinstitutionalization.

The trouble is not in these several programs per se but rather in the confusion, by policy makers and systems planners, of these programs with mental health systems. Outcomes in these subsystems are obviously not the same as outcomes in the greater mental health system. And outcome measures that are appropriate for one are not suitable for the other.

Conclusions and Recommendations

The foregoing discussion leads logically to several summary conclusions and recommendations.

First, we must confront our conceptual and definitional problems so that interventions in the community treatment of chronic mental patients may be placed in perspective. To the extent that organic community support systems exist in reality, each is a local and idiosyncratic method of dealing with the problems of the chronically disabled and, as such, is unique. Hence, we may look to them to provide us with broad guidelines in service planning, but their generalizability is severely limited. They lack experimental specificity and cannot be replicated.

Second, it is possible to deal with some issues in community support programming by investigating outcomes in programs set up as experimental alternatives to hospitalization. Although these programs differ from organic community support systems, they may serve as substitute laboratories. These programs may be viewed as synthesized community support systems in that they appear—insofar as it is possible to make such a determination given an essentially nonspecific definition—to honor the various criteria used in determining community support systems as promulgated by NIMH.

Third, outcome studies of the effects of synthesized community support systems on chronic mental patients show these efforts to be at least as effective as in-hospital programs in some particulars of patient care, and more effective than in-hospital programs in others. However, the documented benefits of these programs are modest and tentative. What advantages do accrue to patients as the result of their enrollment in these programs are apparently of a temporary nature and appear to be sustained only so long as direct and aggressive interventions by program staff are pursued. It must be recognized also that the methodological problems associated with assessing outcomes in synthesized community support systems are sufficiently serious to warrant only the most cautious acceptance of these results.

Fourth, outcome research in synthesized community support systems is best suited to matters concerning patient care techniques—questions about the specific treatments and environmental circumstances that most effectively meet the needs of specific categories of patients. Research directed toward these kinds of questions should continue, and new directions should be encouraged. It is essential that immediate efforts be launched to minimize the extensive methodological difficulties that now confound such research. New and more valid outcome measures are needed, as are more rigorous study designs that would foster improved cross-study comparability.

Fifth, because patient-centered investigations may deflect attention from the broader policy questions surrounding deinstitutionalization, they should be supplemented with other kinds of outcome research. Outcome studies of synthesized community support systems largely ignore, or are irrelevant to, the global problems of deinstitutionalization. Accordingly, we would be well served by attempting to investigate the outcomes of deinstitutionalization more directly.

One approach that holds promise lies in the application of systems theory. According to Miser (1980), systems theory asks questions that involve the critical examination of the social purposes of an intervention, that explore alternative ways of achieving goals, and that estimate the "impacts of various courses of action" (p. 145). Systems theory is implicitly interdisciplinary and comprehensive in its approach (Weiss 1967; Marmor 1975; Holder 1977; Engel 1980; Stratas and Boyd 1981).

The literature is now just beginning to explore some systems issues that must be resolved if deinstitutionalization efforts are to meet with success, and chronic mental patients are to be cared for humanely in community settings. Bradley (1976) shows, for example, that deinstitutionalization involves both program development objectives, such as establishing a system of community-based care, and program termination objectives, such as phasing out institutional care. The two objectives need not necessarily be met simultaneously, and it is possible to vary the speed and completeness with which each is implemented. But because strong partisan views have prevailed, and because economic resources are scarce, these two potentially autonomous processes have become linked, and scholars like historian David Rothman are quoted as saying that "'there is good reason to believe that deinstitutionalization and State mental hospitals cannot coexist'" (Sargent 1980). The implication here is clearly that disengagement from institutional care must be total and immediate.

Systems theory would permit the theoretical and practical separation of these two objectives, so that priorities could be set and intermediate goals could be effected. In fact, Bradley (1978) provides a most insightful discussion of the steps that must be followed in making critical choices in the formulation of public policy. She writes:

> Since all ends and needs are not equal or equally met, these choices must be among competing priorities and should be closely tied to political and fiscal exigencies. . . . [A plan for effecting changes in policy] when viewed in this light forms the impetus for change and bridges the gap between ideology and implementation. [p. 52]

Although the service delivery options being tested in synthesized community support systems may hold the key to future planning for direct patient care, they are not immediately translatable into public policy decisions. They represent but one kind of needed outcome study and must be supplemented by impact analysis in order for the deinstitutionalization movement, and its overall benefits and limitations for persons with chronic mental disorders, to be assessed completely and objectively.

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Conference on Schizophrenia Studies and Aging

The National Institute of Mental Health (NIMH) Center for Studies of the Mental Health of the Aging, in collaboration with the Center for Studies of Schizophrenia, will be sponsoring an open conference on **Schizophrenia, Paranoia, and Schizophreniform Disorders in Later Life** to be held at **The Jack Masur Auditorium, National Institutes of Health Campus, Bethesda, Maryland, June 7–9, 1982.** The conference will focus on two major populations: (1) individuals diagnosed schizophrenic in early adulthood who are presently entering old age; (2) individuals who have experienced the first onset of symptoms in later life.

Although schizophrenia has traditionally been studied as a psychiatric disorder with onset in early adulthood, there exists little systematic knowledge regarding the changes in course, treatment, or prognosis of this disorder which accompany advancing chronological age. Moreover, numerous questions remain regarding the viability of diagnostic classifications such as "paraphrenia," or "late-onset schizophrenic states." The reliable distinction of such disorders from paranoid states and from progressive dementias and other forms of cognitive impairment associated with advancing age require further systematic attention.

The conference will focus on:

- Stimulating increased interest in these substantive areas.
- Reviewing the state of the art.
- Specifying precise substantive recommendations to NIMH for research program development.

If you have worked clinically with either one or both of these populations and would be interested in sharing your research perspectives on these issues with us, we would be pleased to hear from you. Empirical data regarding epidemiology, assessment, differential diagnosis, biological, or sociocultural parameters of illness, and treatment modalities are especially welcome. Please address your correspondence to:

Dr. Nancy Miller
Center for Studies on Aging
National Institute of Mental Health, Room 11A-16
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Rockville, MD 20857

Assessment of Social Skills

by Robert Paul Liberman

Abstract

Deficiencies in social skills, important in the functional adjustment and rehabilitation of persons with schizophrenia, derive from inadequate learning experiences, disuse, anxiety, cognitive disturbances, and amotivational states. Social skills training programs should be specifically organized to compensate for these varied sources of deficiency in interpersonal competence. Assessment of social skills deficits can proceed along topographical, functional, and information-processing lines. Assessment technology is in its early stages of development and will require attention to the psychometric properties and multidimensional focus of evaluative instruments.

Tom was first referred for psychiatric treatment at the age of 15 when his teachers noted that he remained totally aloof from his classmates, rocked in his chair and talked to himself. He responded to questions in a monotone and with monosyllabic answers. When relatives or nursing staff attempted to engage him in conversation, his rocking increased in speed, he bit into his fingers, and he destroyed his clothing and nearby furniture. He moved from one psychiatric hospital to another, deteriorating in his personal habits and social behavior.

* * * * * * * * * *

Jim had his first hospitalization after a year's service in the Peace Corps. His supervisors noticed growing depression, withdrawal, and suspiciousness in Jim and when he was examined by a psychiatrist, he verbalized delusions of being controlled by the CIA. After a 3-week hospitalization with neuroleptic drug therapy, Jim gradually recovered his friends and returned to a job. His main complaints, during the next two years, were easy fatiguability, depression, and dry mouth, a side effect of his maintenance neuroleptic drug therapy. He lived at home with his parents and participated actively in family, church, and social functions.

* * * * * * * * * *

Carl drifted in an apathetic life style for a year after his discharge for a florid schizophrenic episode with auditory hallucinations and incoherence. He spent his days lying on the sofa at home watching TV. If his sister did not wake him up and drive him to the day treatment center, he did not go. Shortly after meeting a girlfriend who was well organized and supportive, Carl found a part-time job, took an interest in his appearance, purchased new clothes, and began working out with weights. He moved out of his family home and found a roommate. For the first time in almost 2 years he seemed "alive," energetic, and goal-directed. This lasted about 2 months. In quick succession, he got the "flu," lost his job, broke up with his girlfriend, and grieved the accidental death of a friend. While agreeing to increase his dose of neuroleptic medication, Carl surreptitiously stopped taking it. Within a few weeks, he became psychotic and was rehospitalized.

* * * * * * * * * *

After three hospitalizations during a 2-year period for religious, persecutory, and grandiose delusions and tactile and visual hallucinations, Ted seemed to "pull together." He got a job as a mechanic, rented an apartment and found new friends. He reduced his contacts

Reprint requests should be sent to Dr. R.P. Liberman, Rehabilitation Research and Training Center in Mental Illness, Brentwood VA Medical Center, 11301 Wilshire Blvd., Los Angeles, CA 90073.

with his parents which had been stormy and marked by criticism and overinvolvement. When he lost his job because of an economic recession, he pounded the pavement until he found another one. When he and his father quarreled over his access to a $2,500 bank account, they negotiated their differences with the help of a social worker until a satisfactory compromise was worked out. His neuroleptic medication was gradually reduced and then discontinued. Three years later, Ted has had no return of symptoms and is planning to marry.

* * * * * * * * * *

John was raised by his widowed father in a decrepit, cold water flat in a blighted area of the city. He was embarrassed to bring his school chums to his home because of its unpleasant atmosphere. While he tried to make friends, he found over the years that they tended to exploit him for favors and money with little reciprocity. At the age of 25 he began believing that he had a special mission and that his actions were being controlled by forces from outer space. He dropped out of his factory job and entered a psychiatric hospital where he was diagnosed as suffering from schizophrenia and treated with neuroleptic drugs. In the hospital, he rarely left his ward. His relationships with nursing staff were marked by extreme docility and dependency. He approached staff members only to have them satisfy some basic, personal need; for example, after 2 days of almost total self-isolation, he approached a nurse and asked her if she would sew a button on his shirt. He retired to bed early and pulled the bedclothes over his head, thereby effectively shutting out the world.

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Each of the above individuals experienced symptoms that are characteristic of schizophrenia and each received the diagnosis of schizophrenia during their hospitalizations. Yet, they are more different than similar in their adaptation to their worlds and in the course and outcome of their illnesses. While biological vulnerability, central nervous system dysfunction, and responsiveness to neuroleptic medication are presumed to influence interindividual variability in schizophrenia, another source of variability likely stems from the social skills possessed by individuals suffering from schizophrenia before, during, and after periods of psychotic decompensation. Admittedly, the evidence pointing toward a relationship between social skills and course of schizophrenia is largely indirect, inconclusive, correlational, and based upon retrospective analyses; however, for heuristic reasons we will assume that social skills do exert a significant influence on the onset, prognosis, course, and outcome of schizophrenia (Liberman et al. 1980).

What Are Social Skills?

Before reviewing the ways in which social skills have been operationalized and assessed, it is necessary to outline a conceptual framework for understanding what is meant by social skills. Social skills refer to the everyday conversations, encounters, and relationships that people have with each other. Social skills include the ability to give and obtain information, and to express and exchange attitudes, opinions, and feelings. Thus, a major function of social skills is to subserve interpersonal interactions. Social skills refer to the nature and function of communication between people.

Behavioral scientists have dichotomized social communication into two major spheres, based upon the interpersonal needs served (Bennis et al. 1964). One sphere is the *instrumental*, where social interaction serves to gain tangible ends that are required for physical, material, and financial well-being. Instrumental relationships have as their function the performance of tasks and the achievement of productive goals. Work and service relationships primarily subserve instrumental role needs. Such interpersonal relationships as boss-employee, conductor-violinist, clerk-customer, agent-client, and doctor-patient serve instrumental goals. Even within families, portions of the relationship between spouses or between parents and offspring serve instrumental role purposes—for example, when spouses discuss the division of labor in carrying out household maintenance tasks. The nature and quality of any interpersonal relationship affect and are affected by the attainment of goals and completion of tasks, but the goals and tasks are the central concerns governing instrumental interactions.

Examples of instrumental situations are:

purchasing an item in a store;

asking for directions for a bus trip;

requesting a job promotion or salary raise;

complaining about side effects from a drug and asking for amelioration from one's physician;

giving information about work experiences at a job interview;

- inquiring about an apartment for rent;
- talking with a social worker about social security benefits.

Instrumental situations require interpersonal communication of varying degrees of complexity, intimacy, duration, and frequency. Some situations can be managed with a single, brief question while others may require repeated interactions, some with great intensity of expression, over a long period of time.

The second sphere that encompasses human interaction is the *social-emotional* one. In social-emotional situations, individuals are not aiming to acquire information or tangible gains that will improve their physical or economic well-being, but rather are aiming to meet their affiliative needs through making acquaintances, conversing with friends and relatives, exchanging emotions and experiences with intimates, and interacting with members of their immediate household. A social-emotional relationship is formed solely for the purpose of fulfilling itself—such as love, marriage, or friendship. The transactions in such relationships are information, opinions, and feelings that are not necessarily aimed at accomplishing some tangible goal. Social-emotional interactions deal with expressions of love, hate, ambivalence, alienation, sadness, happiness, joy, and wishes.

Examples of social-emotional situations are:

- asking one's spouse how he/she feels;
- disciplining one's child;
- greeting a friend with a hug and a smile;
- complaining to one's spouse about feeling tired or ill;
- going to a show with a friend;
- asking one's neighbor who he/she will vote for;
- exchanging comments with an acquaintance about the weather or sports.

The major targets or goals of social-emotional situations are to acquire, make more intimate, and maintain friendships and family relationships.

Obviously some interpersonal interactions subserve both instrumental and social-emotional functions, such as when a father praises his child for carrying out a chore or errand. It is not the interpersonal "other" that defines the nature of the interaction, but rather the primary function of the specific interaction for the individuals concerned. In some situations, one person is obtaining gratification of instrumental needs while the other person is obtaining social-emotional satisfaction. This can occur when a person agrees to drive a neighbor to the hospital on an emergency and receives thanks and gratitude in return. The driver has succeeded in strengthening the friendship ties with his/her neighbor (social-emotional needs) and the neighbor has obtained needed medical care (instrumental needs). The family in previous generations and in more traditional societies, satisfied both instrumental and social-emotional needs. In recent years, however, the family has satisfied fewer instrumental needs since geographical and social mobility as well as other institutions have preempted the work and economic functions of the family.

In summary, we can divide most if not all of interpersonal interactions into the instrumental and social-emotional categories according to the functions or human goals they subserve. This is an important distinction to make since it affects the way in which social skills are to be assessed and trained. We will now take another step toward defining social skills by developing categorical ways of viewing interpersonal interaction. Each of these viewpoints can be used for evaluating instrumental and social-emotional situations. The conceptual categories of social skill are (1) topographical, (2) functional, and (3) information processing. These three categories are not mutually exclusive but, rather, provide concurrent, multidimensional ways of objectifying the abstract concept, social skills. Each dimension or category, by itself, has limitations of validity.

Topographical View of Social Skills

> John appeared disheveled and stooped over with his shoulders hunched together. He rarely made eye contact, except furtively. He greeted others reluctantly with a limp handshake, and answered questions as often with a grunt or nod as with words. The content of his conversation was liberally sprinkled with negative selfreferences and pessimistic expressions of hopelessness for the future. The nursing staff could not remember the last time they observed him smile.

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The topography of social skills includes the verbal content and nonverbal elements in person-to-person communication. Colloquially we are familiar with the importance of verbal content in making assessments of a person's social competence since we designate socially skillful individuals as "articulate" and "verbal." In the verbal dimension we are concerned with the individual's choice of words and phrases in the communication effort. For example, the individual who can put his feelings into words, rather than "act out" his feelings, is considered more socially appropriate and competent. Some clinicians have observed that psychosomatic patients have great difficulty in being aware of and expressing their feelings and have labeled this deficiency, "allexithymia."

The verbal and semantic components of communication have been operationalized in a variety of ways, primarily on the basis of face validity and ad hoc assumptions about what is considered "socially skillful." Individuals who refuse to comply with unreasonable requests and who initiate requests for changes in others' behavior to gain a desired goal have been viewed as more socially skilled than individuals who show compliance and passivity. Offering praise and appreciation when it is deserved in an interaction—such as saying "thank you" when complimented—is considered a sign of social skill from the topographical point of view.

In addition to the verbal content of speech and how words and phrases are related semantically, the topographical definition of social skills also includes the paralinguistic or nonverbal elements of communication. These have been studied extensively by social psychologists, ethologists, and communication theorists and include many components of interactive style that give connotative meaning to what is being said. For illustrative purposes, these paralinguistic and nonverbal elements are listed in table 1, together with normative indications for their being considered socially skillful. Comparative studies have found that some of these nonverbal elements are abnormally excessive or deficient in schizophrenics and other chronic mental patients when compared with normals (Eisler et al. 1975; Hersen et al. 1978). Similarly, patients who received social skills training significantly improved their performance of the nonverbal behaviors that were targeted for training and showed higher levels of performance than patients who did not receive training (Goldsmith and McFall 1975; Bellack et al. 1976).

However, the molecular, topographical approach to defining social skills is beset by questions about its validity. As pointed out by Bellack (1979, p. 169):

> it is not at all clear which components are worth assessing. The customary target behaviors have been selected on the basis of face validity and of the voluminous social psychology literature on interpersonal behavior. The tenuous nature of face validity is self-evident . . . and much of the social psychology literature is based on a laboratory model in which specific response components are studied in isolation, out of the normal context and combinations in which they occur. While eye contact, voice volume, or hand gestures might be important when all other aspects of interactive behavior are held equal, interactions in the real world are rarely so simple or clearly differentiated. . . .

In addition, a number of studies have failed to establish the external validity of these molecular, topographical components of social skills. For example, while the global ratings of social skill of chronic psychiatric patients in group therapy and structured interviews were moderately correlated, there was little relationship between these two evaluation situations and the molecular verbal and nonverbal ~~components displayed~~ by the same patients in role play situations (Bellack et al. 1979). In a followup to this study, Bellack (1979) found little relationship between molecular behaviors rated in role-playing exercises and other measures of interpersonal behavior rated during naturalistic interactions. While the overall contribution made by topographical research on social skills is suggestive, its cumulative impact is not

Table 1. Paralinguistic and nonverbal elements

Nonverbal elements	Indicative of "social skill"
Duration of verbal response	Longer duration
Latency of verbal response	Shorter latency
Dysfluencies and pauses in speech	Fewer speech disruptions
Smiling and facial expression	More smiling
Loudness of speech	Louder speech
Intonation of speech	More accents and variation in tone
Eye contact	Greater eye contact
Posture	Mobile and open posture
Hand gestures	More appropriate gestures

yet sufficient to establish the criterion validity of these molecular verbal and nonverbal components.

Functional View of Social Skills

> When John was offered vocational rehabilitation counseling, he appeared uninterested and had to be escorted to the sessions. While he had considerable savings in his bank account, he repeatedly forgot to get to the bank in time and resorted to "begging" other patients and staff for cigarettes and other personal needs. He did, however, assert his desires to meet with his psychiatrist and would engage the latter in long discussions about trying different drugs or combinations of drugs.

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An alternative view of social skills begins with the assumption that attainment of instrumental and social-emotional goals reflects competence and adaptation. Individuals who can satisfy their material and physical needs through instrumental role functioning are considered socially skilled. Similarly, individuals who can meet their needs for conversation, companionship, nurturance, and affection through friendships and family relationships are considered socially skilled. Thus, the ability to return an item of defective merchandise with a refund or the ability to obtain a job in a competitive employment situation would be considered instrumental social skills. The ability to acquire friends and maintain intimacy over time would be considered indicators of social-emotional skills. A caveat in this view is that such instrumental and social-emotional needs and goals must be met without violating the rights and needs of others. For example, a nursery school child who monopolizes teacher time and toys, at the expense of peers, cannot be considered "socially skilled" despite temporarily achieving goals.

The functional definition of social skills focuses on the outcome of the interaction between "actor" and "respondent," as reflected in the achievement of the "actor's" instrumental and social-emotional goals. Achievement of goals, however, is often dependent upon the attitudes, feelings, and needs of the "respondent," particularly in reaction to the "actor." This consideration of the two-way, interactive framework of social skills is implicit in definitions of social skill that have been offered by workers in the field.

> Social skill is the ability to elicit social reinforcement from others. [Doty 1975, p. 679]
>
> Social skill is the ability to maximize the strength of punishment from others. [Libet and Lewinsohn 1973, p. 311]

The likelihood of achieving one's goals is markedly enhanced if the individual grasps and makes use of generally accepted social norms and expectations. The reactions and readiness of others to respond favorably (i.e., to give positive reinforcement) to an individual will depend in large measure on the individual's ability to "read" the social context accurately. Here is where the *timing* of a social initiative is important. For example, in one study of male college students who rated themselves as heterosocially anxious or nonanxious, both groups supplied an equal number of positive statements to a female confederate, but the nonanxious students were more proficient in their timing of positive feedback. The absolute quantity or quality of verbal and nonverbal responses may be less important than when the responses are made. Two individuals who use identical styles for entering into an established conversational group may have differing success depending upon the timing of their entry. Attention must be paid to the interactive sequencing of verbal and nonverbal communications, such as by analyzing the conditional probability of responses given different antecedents and contexts.

The importance of familiarity with the "rules of the game," together with topographical and functional aspects in determining social skill, can be highlighted by a transcultural example. In the United States or Western Europe, a relative in mourning at a funeral would be considered deficient in emotional skills for failing to exhibit signs of grief and sadness. On the other hand, in Japan, a mourner who cried in public at a funeral would be considered gauche and inappropriate—the time and place to grieve for Japanese is in the privacy of the home with only the immediate family present. In every culture there are rules governing social behavior in most common situations. In a similar vein, bodily contact between friendly males is commonly accepted and valued in Arab and African cultures, but would be viewed as an indicator of sexual intimacy in Northern Europe or the United States. Barker and Wright (1955) found that in a town in Kansas there were over 800 standard "behavior settings"—going to church, interacting in the drug store, conversing on the street—with each of these settings having its own rules for social conduct. People are not ordinarily consciously aware of these rules; that is, the rules often remain implicit and are sensed mainly when violations occur in their adherence.

The inclusion of the *reactions of others* and the *social norms* in an expanded conceptualization of social skills that also takes into account the *topographical* and *goal-attainment* or *functional* views is illustrated by two of the most comprehensive definitions of social skills:

> [Social skill is the ability to] express both positive and negative feelings in the interpersonal context without suffering consequent loss of social reinforcement. Such skill is demonstrated in a large variety of interpersonal contexts and involves the coordinated delivery of appropriate verbal and nonverbal responses. In addition, the socially skilled individual is attuned to the realities of the situation and is aware when he is likely to be reinforced for his effort. [Hersen and Bellack 1977, p. 512]
>
> [Social skill is the ability] to understand other people's use of elements of expression . . . convey impressions through appropriate verbal and nonverbal behaviors . . . to affect behaviors and feelings of others in ways the person intends and which are socially acceptable . . . to influence the environment sufficiently to attain basic personal goals. [Trower, Bryant, and Argyle 1978, p. 2]

Particularly important for chronic mental patients is the accurate perception of social situations which enable them to respond appropriately. Inappropriate affect and behavior are perhaps the prime reason for the alienation and stigmatization of the chronic mental patient. In part, these deficiencies result from long years of institutionalization during which the norms of the hospital, where "crazy behavior" is expected, supplant the norms of society. Among the social-emotional situations that cause problems for schizophrenics and other chronic patients is the arena of self-disclosure. Many patients, conditioned by the expectations for open revelations of symptoms and distress in psychiatric settings, inappropriately generalize these expectations to the community. Self-disclosure is an important verbal skill in the acquiring and deepening of friendships; however, if the timing and context are poorly appreciated, premature and excessive self-disclosure may lead to rejection by others.

Information-Processing View of Social Skills

> John claimed that treatment staff members at the psychiatric hospital were angry with him, despite their persistent efforts to reach out to him supportively. He misperceived potential acquaintances as rejecting him, when actually most people were indifferent to him because of his passivity. He had great difficulty thinking of any alternatives for spending his weekend leisure time, and usually ended up sitting at home alone. At one point he asked the social worker if she could find him a board-and-care home to which he could be discharged. She arranged for him to have an interview at one place and emphasized the importance of his looking his best. When she arrived, his hair and pants were dirty and there was no time to clean up. They went to the interview and John was told by the manager of the home to "think it over and call back if interested." A week later, John told the social worker that he had misplaced the phone number of the home but still wanted to move there. When the social worker asked him what he could do about the situation, John was at a loss for words. When she gave him the phone number and a coin to make the phone call, he insisted that the operator of the home would be angry if he called and that his only option was to stay in the hospital.

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Building on the topographical and functional definitions described above, researchers have added an information-processing and problem-solving view to produce an overarching approach to social skills that has particular relevance to the schizophrenic because of its emphasis on cognitive functions. Guilford (1967) proposed that social skills involved several elements of "behavioral cognition." Based on the results of a factor analysis of several tests of social intelligence and verbal comprehension, Hoepfner and O'Sullivan (1968) identified six orthogonal factors of behavioral cognition that were independent of verbal comprehension. These factors included abilities such as the correct recognition of gestures and postures as expressions of thoughts and feelings; resolving contradictory information received from two modes of expression; comprehending a sequence of social events; and predicting the consequences of a social situation. General intelligence did seem to be a moderator variable in the sense that individuals who had high intelligence test scores generally had high behavioral cognition scores, while individuals with low intelligence test scores had either high or low behavioral cognition scores.

Spivack, Platt, and Shure (1976) defined social skills as "interpersonal, cognitive problem-solving skills." They identified six skills: problem recognition, means-ends thinking, alternative thinking, causal thinking, perspective taking, and consequential thinking. In a series of studies, they found that psychiatric patients generate fewer means to achieve a goal than do normals. Within a group of 190 psychiatric patients, poorer problem-solving skills were associated with high scores on the Sc and Pa scales of the Minnesota Multiphasic Personality Inventory (MMPI), and poorer premorbid social competence. However, patients did not differ from normals in the ability to recognize correct solutions to interpersonal problems.

Trower, Bryant, and Argyle (1978) developed a comprehensive information-processing model to describe socially skilled behavior. First, they hypothesized that social behavior is initiated and maintained by an overall goal with a set of subgoals, united by a plan of action. To implement this plan of action, the "actor" must first perceive the relevant characteristics of the interpersonal situations, translate these perceptions into possible courses of action, decide which course of action is best, and then implement the chosen action through a series of discrete motor responses. Feedback from the environment begins this process again. Based on this model, Trower, Bryant, and Argyle (1978) constructed 51 exercises to teach patients observation skills, listening skills, and speaking skills.

At the Camarillo/UCLA Mental Health Clinical Research Center for the Study of Schizophrenia, a research group led by C.J. Wallace independently developed a similar information-processing model of socially skilled behavior (Wallace 1978; Wallace et al. 1978, 1980). They theorized that a socially skilled response is the end result of a chain of behaviors that begins with accurate "reception" of relevant interpersonal stimuli, moves to flexible "processing" of these stimuli to generate and evaluate possible response options from which the correct one is chosen, and ends with appropriate "sending" of the chosen option. Based on a survey of the literature on interpersonal problem-solving skills, they identified a set of potentially important variables for "receiving," "processing," and "sending" functions. These variables and their employment in assessment and training of social skills are shown in table 2.

Table 2. "Receiving," "processing," and "sending" variables in an information-processing conceptualization of social skills assessment and training

"Receiving" phase	
Assessment	**Training**
Who is in the scene? Where is the situation? What was said by the others in the scene? Who wants what from whom? Which emotions were expressed?	Focus attention and use attentional exercises Prompt correct answers Model correct answers Reinforce correct answers
"Processing" phase	
Assessment	**Training**
Define goals, rights, and responsibilities Generate response alternatives Anticipate and evaluate consequences Choose a response	Adopt a "problem-solving set" Prompt, model, and reinforce problem-solving strategies Practice problem-solving through exercises
"Sending" phase	
Assessment	**Training**
Verbal content Nonverbal components Timing and context Reciprocity	Behavioral rehearsal Modeling Prompting and cueing Positive feedback Self-instructions and self-reinforcement Practice in vivo

Methods of Assessing Social Skills

The behavioral and social learning approaches to clinical problems, such as social skills deficits, emphasize a fundamental *integration of assessment with therapeutic or educational efforts*, and a *multilevel* or multimethod approach to assessment. Intrinsic to behavioral therapy and training approaches is ongoing evaluation of progress, which then provides a feedback loop back to the clinician. The behavioral assessment strategy is to employ multilevel and multimodal measures that tap the subjective experience of the patient (affect, cognition, imagery, sensation), the observable behavior of the patient (verbal and nonverbal responses), and in some cases the physiological or biological level (electrodermal response, electromyographic response, hormonal levels). In the field of social skills assessment and training, measurement primarily focuses upon subjective responses and overt behavior and its consequences.

Beyond the assessment of the ongoing progress and changes in the patient's subjective and overt behavioral responses to social situations, the clinician and researcher is interested in evaluating *generalization* of the skills into untrained and novel situations, and *durability* of any skills that have been acquired. A final assessment goal is to determine whether the learned social skills will "strengthen" the individual and make him less *vulnerable* to those life events and stressors that can provoke relapse. Thus, an assessment strategy must be able to determine which levels of social skill change with training; whether the changes are of sufficient scope and amount to enable the individual to interact successfully in naturally stressful situations; whether the patient can use the newly acquired skills in novel settings to solve interpersonal problems; whether the skills remain in the person's repertoire over time; and whether the skills protect the person from symptomatic relapse and psychosocial deterioration.

There are a number of questions that arise when one begins to develop an assessment strategy for social skills:

What types of responses should be measured?

- internal states and subjective experiences;
- verbal and nonverbal elements of behavior;
- completion of functional interpersonal goals and tasks;
- frequency of interaction or extent of avoidance;
- social anxiety and discomfort;
- degree of compliance with social rules.

Who should conduct the measurements?

- the patient;
- the others interacting with the patient (e.g., confederates and interviewers);
- uninvolved trained observers.

What situations should be used for assessments?

- interactions with intimates;
- instrumental and task situations;
- problem-solving situations;
- initiating or terminating interactions
- positive or negative assertion situations

What framework should be used for the assessment technology?

- self-report questionnaire;
- interview;
- naturalistic in vivo observations;
- confederate tests;
- role play situations;
- permanent products of interactions

While it would be ideal to measure social interactions reliably as they spontaneously occur in natural settings, this technology is rarely economically or ethically feasible. Many important social interactions occur unpredictably in response to infrequent but intense challenges and provocations and, hence, cannot be easily scrutinized. Some situations are intimate and private events that do not permit the presence of outside observers. There are occasional approximations that can be made to carrying out direct observation of social behavior in natural settings (e.g., observing a patient in a waiting room social situation, or observing spontaneous interactions on a hospital ward), but for the most part assessors have had to compromise by relying on "second best" methods of measurement. These "second best" methods are not mutually exclusive since they are each designed to tap different levels of social skill. (See table 3.)

Advantages and Limitations of Assessment Technology

While these methods have been used reliably and productively by investigators who have developed our initial data base on social skill assessments, they have been marked more by face validity and consensual validity than by systematic analysis of their psychometric properties. For example, self-report inventories have been constructed in different ways, with some eliciting responses focusing on social anxiety and others focusing on social effectiveness. Researchers who have developed self-report inventories have tended to agree much more on the content of the questions than on how the questions are asked or how the answers are framed. Some inventories have used "true-false" and "yes-no" formats while others use Likert-type scales. The questions or items are open to idiosyncratic interpretation because of the lack of space and time for elaboration of instructions, and the ambiguity of the questions. At the MHCRC for the Study of Schizophrenia, we have noted that our schizophrenic subjects have uniformly abhorred the self-report inventories related to social skill. They have found them confusing and difficult to answer; hence, we have experienced a high refusal rate in repeated administrations of the inventories, and for those who have complied with the task, they have done so perfunctorily and with obvious unreliability.

Table 3. Methods of measuring social behavior

Measurement technology	Types of social behavior measured
Self-report questionnaire	Social anxiety or comfort "During an argument I am sometimes afraid that I will get so upset that I will shake all over."
	Social approach or avoidance—frequency "I have hesitated to make or accept dates because of shyness."
	Social difficulty or ease "I enjoy starting conversations with new acquaintances and strangers."
	Perceived effectiveness of social interaction "When I have done something important or worthwhile, I manage to let others know about it."
	Positive assertion "Do you tell your friends you care for them?"
	Negative assertion "Are you usually able to say 'No' if people make unreasonable requests?"
Interview	All of the above
	Ratings of the interviewer Verbal and nonverbal behavior of patient (competence and comfort as perceived by interviewer) Subjective reaction by the interviewer
Role-play tests	Social perception
	Cognitive processing Generating alternatives Weighing consequences Choosing a reasonable option
	Nonverbal communication Duration of reply Latency of response Duration of eye contact Speech dysfluencies
	Compliance content and requesting a change in others' behavior—negative assertion
	Praise, approval, appreciation, and acknowledgment—positive assertion

Role-play tests have the advantage of clarity and specificity in the instructional sets provided to the patients. While schizophrenic patients are more likely to comprehend the lengthier instructions given directly or through a standard audiotape than they are the written instructions for a paper-and-pencil questionnaire, some individuals experience awkwardness and embarrassment in complying with the role-play expectations. The social performance anxiety associated with the

Table 3. Methods of measuring social behavior—*Continued*

Measurement technology	Types of social behavior measured
Role-play tests (continued)	Social rules
Naturalistic interactions	Competence and comfort of the patient as globally perceived by the confederate
	Completion of specific tasks and assignments
	Subjective reactions to the patient by the confederate "When I am with this person, he makes me feel distant from him."
Permanent products	Tangible indicators of completion of tasks or entry into certain situations Ticket stubs, salary stubs, job application Written reports on the completion of interpersonal assignments by the significant other involved in the assignment (e.g., teacher, parent)

"testing" qualities of the role-play situation may interfere with the patient's full demonstration of social skills.

However, role-play tests of social skill offer researchers a standardized, easily replicable assessment situation. The interpersonal tasks and challenges posed by the role-play test can be generated in quantity, with judges rating each task for degree of difficulty and type of skill, thereby enabling different task situations to be used for pre- and posttesting after a period of training. This interchangeability of the scenes or tasks reduces the biasing of practice effects. Role-play tests also provide opportunities to assess both discrete component behaviors of social skill (e.g., duration of eye contact) as well as global features (e.g., ratings of overall assertiveness or appropriate affect). Role plays are also convenient to administer and can be harnessed to a measurement approach that uses direct observation, videotapes, and "blind" raters.

On the other hand, role-play tests are handicapped by methodological flaws. The most serious problem with role-play tests lies in their lack of external validity. Since the role-playing situations differ in many ways from the real life situations encountered by the patient, there is no assurance that what is evaluated during the analogue situation in a videotape studio reflects "real life" behavior. For example, the demand characteristics inherent in role-play tests may induce very different behavioral responses than might occur in real life—better or worse, depending on the expectations generated by the patient, the clinician, and the experimenter. Furthermore, the discrete behavioral components of social skill that have been the most frequent targets of role-play assessments bear an uncertain relationship to other criterion measures of social skill. Three recent studies, in fact, failed to find correlations between the paralinguistic and nonverbal behaviors rated from role-play tests with ratings made from more naturalistic situations (Bellack 1979).

Naturalistic interactions encompass simulated or staged encounters which are designed to approximate situational tasks and challenges that are frequently encountered in real life. For example, one research group unobtrusively observed psychiatric patients interacting with a "stranger" in a hospital waiting room. The stranger was, in fact, a confederate of the researchers who was prepared to interact with the patients in a preordained manner (Gutride, Goldstein, and Hunter 1973). The research group at the MHCRC for the Study of Schizophrenia has adopted the naturalistic, conversational interaction described by Goldsmith and McFall (1975). In this assessment approach, the patient is instructed to bring up a popular topic (e.g., sports) at the first pause in the conversation; to offer the confederate (who is introduced as a friend of the clinician or researcher) a cup of coffee; and to terminate the conversation after 5 minutes. On his side, the confederate is instructed to say, after being introduced, "I'm sorry, I've forgotten your name"; to refuse the offer of coffee; and to ask directions to a nonexistent bus stop or building. Thus, the interaction is staged to require the patient to initiate and complete certain tasks, and to cope with mild stressors presented by the confederate.

The naturalistic interactions

have been found to be sensitive to the effects of training in a number of studies; however, the variation among these naturalistic interactions in duration, content of task, stressors, and setting makes comparisons between studies difficult. Major advantages of the naturalistic interaction as a valid form of assessing social skills are the spontaneity induced by its surreptitious nature, and the lengthy exchanges between the patient and the confederate that can occur. Social behavior is *interactive* and is best evaluated by situations that permit conversational partners to take turns in talking and responding over an extended sequence. This enables the information-processing aspects of social skill to become manifest since the patient must use "receiving" and "processing" skills as well as "sending" skills. The naturalistic interaction also permits a wider scope for rating social behavior. Ratings can be made of:

- subjectively experienced affect and subjectively reported estimates of performance (by the patient)
- subjective reactions of the patient's impact (by the confederate)
- perceptions of the patient's anxiety (by the confederate)
- perceptions of the patient's competence (by the confederate)
- global and discrete indicators of the patient's anxiety, and competence (by objective, trained raters from videotapes of the interaction)

In addition, both the confederate and the trained observers working from the videotapes easily can be kept "blind" as to the patient's treatment/training condition.

There are ethical issues that need to be considered since the naturalistic interactions are contrived and the observations are carried out surreptitiously. To protect the patient's rights, it is important that (1) the contrived task not cause undue pain to the subject, (2) the subject be debriefed regarding the nature of the deception, if any, and (3) the subject be given the right to deny the use of the information obtained through surreptitious observation. Without such precautions, such tasks could create a suspicious atmosphere which might cause relationship problems for the patient, the experimenter, and the collaborating clinicians.

Identifying Ecologically Valid Situations for Assessing Social Skills

In the above sections, we have elaborated a multidimensional framework for understanding the concept of "social skills" and described some of the technology used for measuring social skills. A singular lack in the methodology for measuring social skills has been the failure of investigators to obtain ecological validation for the social situations and responses incorporated into self-report inventories, role-play tests, and naturalistic interactions. Social skills trainers have tended to assume, without empirical justification, that certain situations and events were critical to a schizophrenic's adjustment to and survival in the community. Thus, we have seen the familiar litany of situational typologies inserted into questionnaires and behavioral rehearsals—positive and negative assertion, starting conversations, making an appointment with the clinician, dating, and saying "No" to unreasonable requests. With rare exceptions (Goldsmith and McFall 1975), scenes have been chosen for social skills assessment and training that have had only face validity. Because of our failure to test the ecological validity of our choice of target goals in social skills training, it is important to do a better job in selecting interpersonal situations that can be documented as critical to a schizophrenic's functioning and survival in the community.

At the Camarillo/UCLA MHCRC, Wallace (1977) conducted a project to assess situations relevant to successful living in residential care facilities in the community. Five residential care operators and two social workers who were liaisons between the state hospital and these community facilities were interviewed at length to solicit those behaviors and social situations that were viewed as crucial in either the return of patients to the state hospital or the production of discomfort and displeasure in the operators with their patients. A content analysis of the situations generated by this interview revealed two commonly cited problems: (1) A patient believes that his rights have been violated by another patient or by the operator. (2) A patient is accused of violating the rights of another patient or the operator. Based on the content analysis of the interviews, 26 interpersonal situations were constructed.

The five operators and two social workers were again contacted and asked to indicate the "best" and "worst" responses that a hypothetical patient might make to each of the 26 situations. From the numerous possibilities mentioned, five alternatives were developed for each of the 26 situations, and based on the amount of aggression displayed in each response, were classified from "best" to "worst."

The situations and response alternatives were then formulated as a multiple choice questionnaire which was mailed to a random sample of 50 residential care operators in Los Angeles and Ventura Counties who were asked to indicate for each situation the rank order from "best" to "worst" of the five response alternatives. Questionnaires were returned by 37 operators and Kendall's Tau and the mean rank of each alternative were calculated for each situation. Four of the 26 situations were discarded either because their Tau was less than 0.70 or because their alternatives were separated by less than a 0.75 difference in the mean ranks. Thus, situations were constructed which had been specified by the residential care operators themselves as being important for successful living in their facilities. In addition, the operators had suggested the response alternatives and had provided consensual validation of the adequacy of each alternative for dealing with the stressful situation.

The next step was integrating these potentially stressful scenes and their response alternatives into a social skills training framework. Ten situations from the questionnaire were randomly selected and used with 18 patients in a role-playing assessment/training program. The context of each situation was presented by the trainer, and a role model delivered a prompt to "open" the scene. The patient was then expected to respond spontaneously to the prompt and attempt to deal with the stressful situation. After the behavior rehearsal was completed, the patient was asked to (1) identify his rights, duties, and goals prescribed by the situation; (2) generate response alternatives (including the response actually rehearsed); (3) predict the likely consequences of each alternative; and (4) evaluate each alternative as a means of achieving his identified goals.

Results indicated that the assessment/training program was reliable. Across the 10 scenes, scores for individual patients in selecting the "best" to "worst" alternatives were highly correlated ($r = 0.89$) as were the total number of correct answers to the questions administered following the behavior rehearsal. The 10 situations did not differ in their difficulty level. Of course, patients differed significantly in their scores for the spontaneous rehersal ($F = 3.47$, $p < .001$), and in their responses to the postrehearsal questions ($F = 10.78$, $p < .001$).

The goal of this project was to develop an individual problem-solving profile—which could be extrapolated to many dimensions of life outside the situations in residential care homes—that would be directly relevant to social skills training. Efforts to attain this goal have been undertaken by the "Life Skills Training" project at the Sepulveda (California) VA Medical Center, one of the constituent projects within the MHCRC for the Study of Schizophrenia. Under the leadership of M. Brown, A. Munford, and C. Deets, a Life Skills Inventory is under development that would provide an index of the competence and deficits of chronic schizophrenics in diverse, important, daily living situations. The same behavior-analytic procedures used in the development of critical situations from residential care homes, described above, is being used to validate this more comprehensive inventory. The behavior-analytic procedures encompass five stages (Goldfried and D'Zurilla 1969): (1) a situation analysis, (2) response enumeration, (3) response evaluation, (4) development and use of the inventory, and (5) evaluation of the reliability and validity of the inventory.

The first stage, a situation analysis, identifies and describes the important situations in which schizophrenic clients must be competent to maintain adequate functioning for reentering the community. This analysis occurs in four segments. First, a comprehensive list of situational areas or domains requiring competence is drawn from patient records and a review of the literature. These domains include those involving self-care, management of symptoms and medication, nutrition and eating, budgeting and personal finance, use of leisure time and vocational activities, use of transportation, dealing with social agencies, interacting with relatives, and friendship and peer relations.

Second, the list of situational domains provides content for an open-ended, semistructured interview with people having extensive contact with the patient population. Third, these groups (e.g., work supervisors, employment agency personnel, rehabilitation practitioners, relatives, nonrelative caretakers, and ex-patients) are asked what situations were problematic and what coping responses might be effective in those situations. In addition, these people are asked to rate the situations drawn from the literature and patients' records in the same manner. These interview results provide a list of problematic situations for the next phase.

The objective of the second stage of the procedures, response enumeration, is to determine the customary range and sequence of responses made by patients in each of the situations identified in the first stage. Thus, the situations are broken into a series of tasks and a variety of responses (also known as task analysis). The variety of responses must then be ranked in a hierarchy of effectiveness. The literature review, the patient records, and the semistructured interview will have indicated the component responses of the problematic situations.

The third stage involves the evaluation of these responses by people having extensive contact with the patients when they reenter the community (e.g., personnel officers, rehabilitation practitioners, relatives, nonrelative caretakers, other ex-patients, and community members such as merchants). These groups judge both the importance of the task and the degree of effectiveness for each of the enumerated, potential patients' responses. These judgments are used to reach a consensus about response effectiveness classified into three categories: superior, average, and adequate. Those responses about which judges show wide disagreement are eliminated to improve the reliability of the inventory. This phase of the inventory development produces a variety of responses arranged in a hierarchy by level of effectiveness for each situation previously identified.

In the fourth stage, the assessment inventory is developed to allow direct responses that can be assessed through questionnaires, interviews, role-play tests, and naturalistic interactions in each of the life skill domains. The first three stages provide a criterion analysis as well as indicating the content of the items and criteria for scoring the responses. In the fourth stage, the patients are asked to imagine themselves in a real life situation and to demonstrate how they would respond in that situation. Further, they are asked what they were thinking or feeling before, during, and after the task. This stage will translate the concept of competence into an operational definition for each of the important domains of life skills.

The final stage is the evaluation of the assessment instrument. Procedures are used to determine the reliability and the validity of the Life Skills Inventory, such as test-retest, interitem, and interrater reliabilities. Inventory responses made by adequately functioning ex-patients, inadequately functioning ex-patients, and adequately functioning normal individuals are compared to evaluate further which situations and which responses within those situations differentiate the three groups. Based on this information, the Life Skills Inventory can be refined. The desired result is a comprehensive Life Skills Inventory which can accurately estimate a client's degree of competence in common, problematic life situations.

The Life Skills Inventory can be a practical and effective means of evaluating an individual's competence in varied areas of life, and predicting how successful adjustment outside hospital systems is likely to be. In addition, the assessments can be readily integrated into highly individualized social and life skills training programs to increase clients' functioning to a competent level before they are discharged from mental hospitals. Finally, the Life Skills Inventory could provide an empirical means of evaluating treatment effectiveness.

At the MHCRC for the Study of Schizophrenia, instruments like the Life Skills Inventory will be integrated into an individualized social skills assessment/training program for schizophrenics. The focus will be on skill attainment at criterion levels for each patient, based on the specific interpersonal problems facing each patient in the various settings of everyday life. Patients will enter the training sequence at a level commensurate with their skills, with some requiring basic skills acquisition and others beginning at higher levels of skills training. Each patient is to progress at his or her own pace through a four-level hierarchy of skills development—shown in table 4—in areas such as peer and family relations; community living; vocations; and symptom management. The proposed assessment/training program, a personalized system of instruction, is designed to allow a person to progress at a different rate in each of these four areas of skills development. Thus, some individuals will possess adequate independent skills for community life (e.g., purchasing and preparing

Table 4. Areas of functioning and hierarchies of clinical intervention for the Community Living/Social Skills Training Program

Level of training	Social	Independent community living	Vocational	Symptom management
I	Basic social skills training	Sheltered living with specific training in grooming, housecleaning, budgeting, and shopping	Prevocational training	Supervision of symptoms and administration of medication by caretaker plus education in self-management
II	Instrumental skills training	Community living with supportive roommate (daily staff visits)	Sheltered workshop/ volunteer assignment	Fading staff supervision and increasing self-monitoring
III	Conversational skills training	Community living with supportive roommate (occasional staff visits)	Community employment with staff supervision	Peer/family supervision of self-monitoring
IV	Generalizing skills to special problem situations and enhancing social etiquette.	Community living with supportive roommate ("buddy") or living alone	Independent community employment	Independent self-monitoring

food, obtaining transportation, and renting an apartment), but will lack skills for socializing with peers and for obtaining a job. Alternatively, a person may have adequate employment skills, but lack the know-how for coping with distracting and distressing symptoms (e.g., how to obtain psychiatric consultation, how to request changes in medication or antidotes for side effects). The advantage of focusing separately on these various areas of skill development is that a person may reach a plateau in one area while continuing to advance to higher levels in another area. By the end of training, patients should have an opportunity to maximize assets, and move capably into the least restrictive and highest quality environment consistent with their level of skills.

Assessment of Motivational, Affective, and Cognitive Deficits Related to Social Skills

Beyond the ecological validity of the particular situations and interpersonal skills that are earmarked for social skills training, the choice of assessment and intervention targets should also be guided by what is known about the *psychological deficits* that influence and determine a schizophrenic's socially skillful *performance*. The performance of an individual schizophrenic in social situations can be deficient for one or more of the following reasons:

- Lack of appropriate social learning in past experience—this has been referred to as a primary deficit in social skills. The individual was insufficiently exposed to socially skillful models within the family or received insufficient reinforcement or too much punishment for fledgling efforts at communication, interpersonal problem solving, and conversation.
- Loss of previously learned skills as when social skills drop out of a repertoire because of long-term institutionalization or years of sheltered and withdrawn living in the community. This "secondary" deficit of social skills derives, as does the "primary" type, from lack of practice, and deficiencies in the external environment's provi-

sion of models, prompting, cueing, reinforcement, and punishment.

- Excessive anxiety in social situations, a particularly important aspect of the experience of schizophrenics and heightened by histories of "primary" or "secondary" deficits. Anxiety and other dysphoric affects disrupt effective social performance even when the elements of social skills are in the individual's repertoire.
- Deficits in cognitive, information-processing skills.

These include faulty decoding, perceptual, or "receiving" skills; stimulus overload with consequent failure to organize thoughts and actions; insufficient generation of response alternatives when faced with interpersonal problems; and negative expectations about response consequences.

Assessing Motivation as a Precursor to Social Skills

Initial, ongoing, and outcome assessment of social skills should incorporate measures of the motivational state of the patient, especially when it is known that the patient once displayed social competence and suffers from "secondary" deficits in social skills. The motivational state of the patient is always in equilibrium with the richness, availability, and contingencies of modeling and reinforcement in the patient's life space. Hence, a complete assessment of social skills should encompass a survey of the reinforcers accessible in the patient's environment.

Schizophrenics and other chronic mental patients often show a pervasive loss of affective expression, experience, and responsiveness to the activities, events, and rewards that reinforce adaptive behavior in most people. Schizophrenics will frequently describe feelings of emptiness or blandness or even a total lack of feelings—a subjective phenomenon that corresponds with their observably flattened affect. *Anhedonia* is a term coined to describe the lack of pleasure in everyday life experienced by many schizophrenics. With a lack of connection of pleasure and emotional responsiveness to instrumental and social-emotional activities, schizophrenics lose interest in the external world, retreat to fantasies, apathy, withdrawal, delusions, and hallucinations, and have no motivation to pursue goal-oriented activities.

The social anxiety experienced by many schizophrenics leads to an active avoidance of social and therapeutic relationships. The reinforcer that serves as the most powerful reinforcer for most people—social relationships—is nonoperative or even an aversive stimulus for schizophrenics. It is understandable that clinicians—who are subject to feelings of frustration, rejection, disappointment, and, if empathic, even emptiness—are reluctant to work therapeutically with schizophrenics on a regular basis for long periods. But if the fear of relationships and flight from social reinforcers is a major feature of schizophrenia, then a tolerant, nondemanding, and long-term, reliable and trusting relationship with a therapist who can demonstrate human feelings is just what "the doctor ordered" for schizophrenics. On the basis of empirical and clinical studies, the time frame to be expected for building social reinforcers into the life experience of schizophrenics would be a minimum of 6 months and as long as 2 to 4 years for many patients (Liberman et al. 1974; Paul and Lentz 1977).

Although schizophrenics are characterized by a constriction in their range and potency of reinforcers, they can be motivated to participate in social skills training by the creative use of positive and negative reinforcers. Money—a widely accepted, highly normative, generalized reinforcer—has been found to be an effective reinforcer for schizophrenic patients' performance in role playing and carrying out interpersonal assignments (Doty 1975; Wallace 1981). Schizophrenic patients in the Camarillo/UCLA social skills training project received $2 for participating in each day's 5 hours of training and evaluation activities. Together with a heavy emphasis on establishing and maintaining close and collaborative therapeutic relationships, the financial reward helped to limit dropouts to only 2 out of a cohort of 30.

Another unusual source of motivation for use in social skills training comes from the experimental findings on social censure. While criticism and negative feedback tend to be viewed as harmful "no-no's" by behavior therapists, studies conducted on laboratory tasks suggest that when clearly linked to incorrect response, critical feedback helps schizophrenics improve their performance. Two recent studies have demonstrated that exposure to a censured model resulted in positive behavioral changes in the social skills of chronic schizophrenics (Denicola 1979). For censure to be beneficial, it must be presented contingent upon inappropriate behavior. It is likely that pairing praise for appropriate behavior with censure for inappropriate behavior will improve outcomes with schizophrenic patients. Important considerations are the quality of the relationship between the patient and the therapist who is giving criticism, the amount of psychopathology experienced by the patient, and the accurate perceiving and processing of the critical feedback (e.g., the patient will not benefit if the criticism is interpreted in a delusional fashion). A series of controlled, single case clinical experiments with schizophrenic patients indicated that various punishment methods were effective in improving social interaction and rational conversation when positive reinforcers alone had failed (Patterson and Teigen 1973; Liberman et al. 1974; Davis et al. 1976; Fichter et al. 1976).

The use of a reinforcement survey as part of the assessment of patients undergoing social skills training would seem apt. Through interviews, questionnaires (Cautela 1977), direct observations of patients' preferences, and reports from reliable informants, it is possible to piece together knowledge about what does and does not motivate a particular patient. Reinforcement surveys require a listing of people, places, things (e.g., possessions, hobbies, food, drinks), and activities that occur often in the patient's daily life or which the patient would like to increase in frequency. Such surveys can yield useful information for the clinician who is planning a social skills training program and for the experimenter who is interested to see if a therapeutic endeavor has led to a change in the patient's range of reinforcers.

Attempts to measure the reinforcing qualities of a patient's environment also point our therapeutic efforts in the direction of the community. It makes little sense to invest long hours in hospital-based social skills training of the individual, unless the community and its aftercare systems can provide reinforcers and prompts to maintain the patient's progress. Here, then, assessment of quality of life and social support networks overlaps with assessment of social skills. For example, one way to overcome deficits in reinforcers is to use a procedure termed "reinforcer sampling." In reinforcer sampling the patient is systematically exposed to activities, interactions, and people that are not initially reinforcing but with sufficient contact and experience become reinforcing. Aspects of the patient's social and physical environment that have past, present, and future reinforcing properties are crucial to change in the patient and can be evaluated through a survey.

Social Anxiety and Social Skill

In the previous section on the assessment of motivation, we pointed out that social anxiety is widespread as part of the schizophrenic experience and that it interferes with the responsiveness of the schizophrenic patient to social reinforcers. In this section, we describe the need to measure social anxiety as part of the assessment of social skills and the methodological confusion that has existed because of the failure to distinguish social anxiety from deficits in social performance. A personal description of social anxiety by John, our illustrative schizophrenic, graphically reveals the impact his anxiety had on his social performance:

> I wanted to have dates and girlfriends, but I would get too tense to do anything. I joined a computer dating club but never got up the nerve to call any of the girls. Once I planned to attend a dance held in my neighborhood by a social club. I even bought some new clothes for the occasion. But as I walked up to the door of the place where the dance was held, I began to tremble and feel lightheaded. When I put my hand on the doorknob, it slipped because my palm was sopping with sweat. Instead of going in, I turned around, went home, and crawled into bed.

Social and performance anxiety can affect social performance in a number of ways; it can facilitate, impair, inhibit, or disrupt the overt behaviors that constitute social performance. Thus, the quality of social performance and social competence as perceived by observers is, in part, a function of the presence and amount of social anxiety. Conceptually, performance and anxiety in social situations should be assessed separately since they represent different factors that are probably orthogonal. Most of the self-report questionnaires that tap subjective perception of social skills have items which ask patients to describe their perceptions of social performance and the presence or absence of associated anxiety and discomfort. The overall score reported by such questionnaires is a conglomerate of views of performance quality (i.e., competence) and affect (i.e., anxiety). It would be preferable to have the competence and comfort factors from such inventories summarized separately since different intervention strategies could be mounted depending upon the relative extent of competence or anxiety.

The best example of an assessment methodology relying on self-report that does clearly differentiate performance from anxiety was developed by Goldsmith and McFall (1975). These investigators put together, in their study of chronic mental patients' social skills, a comprehensive set of internal state measures that included the Interpersonal Situation Inventory; three additional scales that asked patients to rate their difficulty in meeting and talking to people, their future ability to perform in interpersonal situations, and their feelings of self-worth; and ratings of competence and comfort in actual interpersonal situations that were recently encountered. The Interpersonal Situation Inventory consists of 55 interpersonal situations to which patients responded by indicating their comfort and competence or by indicating that the situation posed by the item was inapplicable to their lives.

Social anxiety can be rated by the patient; by interviewers, observers, or significant others; and by physiological means (e.g., electrodermal response, heart rate, electromyogram). Each of these response modes—subjectively experienced anxiety, observation of overt motoric and verbal signs of anxiety, and physiologically assessed arousal and tension—should be measured to give an accurate picture of anxiety and stress (Lang 1971).

While the assessment of anxiety in clinical situations is appropriate to determine whether anxiety reduction or competence training is warranted, it should be noted that direct training of overtly demonstrated skills can have an anxiety-reducing effect on the patient. Whether or not specific anxiety-reducing methods, such as systematic desensitization or imagery-based flooding, provide an increment of benefit in social skills training programs needs empirical exploration. As the reader familiar with behavior therapy methods will understand, direct training of social skills through behavioral rehearsal, practice, and in vivo assignments contains within its training steps several opportunities for "exposure" to anxiety-evoking situations—the most powerful ingredient of all anxiety-reduction treatment packages.

Cognitive Processes and Social Skill

The most intensively studied psychological aspects of schizophrenics have been their cognitive and attentional deficits. These deficits have been presumed to be fundamental or basic mediators to schizophrenic symptomatology and indicative of the underlying neuropsychological vulnerability in persons predisposed to schizophrenia. The term "cognitive" may refer to all processes by which sensory input is transformed, reduced, elaborated, stored, recovered, and used. This includes processes of sensation, perception, attention, memory, thinking, language, and related verbal and motor responses. It can be seen that these information-processing functions are also important determinants and moderators of social skills.

Subjective reports by schizophrenic patients during their actively psychotic periods highlight the problems experienced with selective attention. They seem overwhelmed by a flood of sensory input that they cannot control. For example, John, our illustrative schizophrenic patient, stated that:

> I have trouble concentrating and keeping my mind on one thing at a time, especially when I'm with people. I can hear what they're saying, but I can't keep up with them and make sense of the conversation. I lose my grip on being a part of the conversation and drift off. It's not so bad when I'm talking with just one other person, but if I'm trying to tune in to a conversation with several people, things come in too fast and I get lost. It's hard for me to contribute to a conversation when the ideas get blurred.

This subjective account graphically illustrates the cognitive problems experienced by schizophrenics in an interpersonal context. During the past 40 years, research in laboratory settings has quantified and categorized cognitive deficits experienced by schizophrenics through a variety of performance tests. Some of the deficits that have been confirmed and replicated are deficiencies in sustaining a focus of attention, distractibility, slowness in the initial processing of information into sensory memory, impaired detection of relevant stimuli that are imbedded in irrelevant "noise," and inefficient organization of information in short-term memory. From this body of research emerges the likelihood that the social skills deficits, as well as the delusions, hallucinations, and thought disorder characteristic of schizophrenia, are mediated by attentional and perceptual dysfunctions which interfere with the integrity of rational, ordered thought, language, and conversation.

Since it is virtually certain that cognitive, attentional and information-processing deficits play an important role in determining the type and intensity of social skills deficits in schizophrenics, it is vital that evaluation of social skills training include measures of cognition and information processing. The inclusion of measures that tap this more basic level of functioning—a level that mediates an individual's adaptation and responsiveness to the social environment—may be more sensitive to the effects of intervention programs. Real effects of intervention programs aimed at social skills may fail to be detected because the outcome measures are too global or fail to assess the levels of functioning that are more proximal to the actual targets for change. The impact of social skills training will be more likely disclosed if the assessment methods used tap the specific cognitive processes that are affected by interventions aimed at improving information-processing and attentional mechanisms. Thus, in addition to measuring multidimensional outcome in the symptomatic, familial, social, community, and vocational spheres, investigators who wish to obtain a comprehensive and sensitive assessment of the outcomes of therapeutic intervention in schizophrenia should also consider the cognitive-attentional sphere. There are reliable and discriminating methods now available for that, including the continuous performance test, short-term memory tasks, the span of apprehension test, the smooth pursuit eye movement test, and various reaction-time tests.

Cognitive Functioning With Social Stimulation

Cognitive and physiological arousal have been hypothesized as mediating the well-described relationship between high levels of social stimulation and symptomatic relapse. Based on research conducted by British investigators at London's Institute of Psychiatry, two complementary processes have been posited to explain the unusual sensitivity of schizophrenic patients to social stimulation (Wing 1978). For schizophrenics living in understimulating environments, such as large, custodial institutions, negative symptoms develop—apathy, social withdrawal, inactivity, and loss of self-care skills. These negative symptoms, or deficits in adaptive behavior, have been termed the "social breakdown" or "clinical poverty" syndrome. On the other hand, overstimulating environments, such as highly critical or emotionally overinvolved relatives at home, or total push, intensive treatment programs, can produce florid psychotic relapses. This dilemma of too little or too much social stimulation has been well described by Hirsch (1976):

> The primary handicap of schizophrenics can be seen as an extraordinary vulnerability, like walking a tight-rope, with the dangers of an understimulating social environment leading to the negative symptoms of social withdrawal and inactivity on the one side, and the dangers of overstimulation leading to florid symptoms and relapse on the other. [p. 461]

Under conditions of overstimulation, a state of central nervous system hyperarousal occurs which increases the danger of symptomatic relapse. For example, schizophrenic patients living with relatives high on "expressed emotion" (i.e., criticism or overinvolvement) tested within their homes showed higher levels of spontaneous fluctuations in the galvanic skin response when their key relative entered the room than did patients with low "expressed emotion" relatives (Tarrier et al. 1979).

High levels of social stimulation could lead to information overload in schizophrenics who suffer from cognitive and attentional dysfunctions. Sensory or information overload could, then, produce the physiological hyperarousal and other neurochemical events which trigger social impairments and symptomatic exacerbation in individuals vulnerable to schizophrenia. The intensity and duration of the noxious social stimulation would determine the type and severity of induced psychopathology. As a speculative example, moderately high levels of social stimulation might induce sufficient cognitive disorganization to lead to delusion formation, while extremely high levels might lead to more thorough-going disorganization and incoherence of thought and speech. Social withdrawal may be an "escape" adaptation by schizophrenics faced with the hyperarousal and information overload inherent in social situations. As Wing (1975) has described the schizophrenic patient:

> If he can't withdraw, if he is forced to interact by a socially intrusive environment, he is bound to show his abnormality in the form of delusions, speech disorder, or odd behavior. [p. 265]

There are empirical data to suggest that cognitive dysfunction is increased by excessive social stimulation in schizophrenia. Sensory input processing has been found to be impeded more significantly by pictures suggesting interpersonal themes of hostility and dependency than by those depicting neutral themes. Intellectual deficits in schizophrenics have been noted to be at their greatest when responses are required to situations with little structure and much reference to personal and social themes. Schizophrenic thought disorder has been found to be more pronounced when the patient is tested making social judgments vs. judgments among objects. The effectiveness of reinforcement in learning tasks has been reduced by the experimenter's presence in the same room with the schizophrenic (Salzinger 1973).

Implications for Clinical Intervention and Social Skills Training

If schizophrenic patients do indeed experience the cognitive dysfunctions described above, then much of the assessment and intervention done to date in social skills training—emphasizing verbal and nonverbal *responding* to social challenges—may bypass the more critical psychological processes that are closely linked with attention, perception, and information processing. Focusing only on the topographical features of social skills—eye contact, gestures, voice volume, requesting the "other" to change, refusing an unreasonable demand—may lead to limited generalization because the cognitive processes that facilitate many different types of socially skilled behaviors in many different situations are not targeted for intervention. Thus, it may be more important to target the sensory input and cognitive processing precursors to verbal and nonverbal output.

Some of the relevant cognitive precursors have been identified by clinicians (Spivack, Platt, and Shure 1976; Trower, Bryant, and Argyle 1978; Wallace et al. 1980). They include "problem recognition," "problem identification," "accurate perception of the relevant characteristics of the interpersonal situation," "knowledge of social mores," "information processing capability," "identifying short- and long-term goals," "generating response alternatives," "weighing the pros and cons of alternatives," "evaluating and predicting potential consequences," "choosing a reasonable alternative," and "implementing an alternative and evaluating its effectiveness in achieving one's goals."

The social skills training program for schizophrenics developed at the Camarillo/UCLA Clinical Research Center (Wallace 1981) represents an important point of departure for clinicians who wish to incorporate cognitive, problem-solving strategies in their social skills training. Wallace and his colleagues theorized that a socially skilled response is the end result of a chain of behaviors that *begins* with accurate "reception" of relevant interpersonal stimuli; *moves* to flexible "processing" of these stimuli to generate and evaluate possible response options from which a reasonable one is chosen; and *ends* with appropriate "sending" of the chosen alternative.

These workers have created an integrated assessment and training package, based on role playing of approximately 200 different interpersonal scenes in areas of hospital, community, friendship, and family relations. After each situation is role played, the patient is asked a series of questions designed to assess his "receiving" and "processing" skills. Errors or deficiencies in these cognitive skills call into action training techniques which are evaluated during the role play and, as in most conventional types of social skills training, are remediated through instructions, modeling, prompts, coaching, and positive feedback.

Meichenbaum and Asarnow (1979) have described similar training paradigms, but for children with academic and behavioral problems. They have carried out "think aloud" training designed to foster each performance-related skill that has been identified through task analysis of the children's situations and goals. Among the skills taught through modeling, prompting, and feedback are:

> (a) problem identification or self-interrogation skills ("What is it I have to do?"); (b) focusing attention and response guidance, which is usually the answer to the self-inquiry ("Now, carefully stop and repeat the instructions"); (c) self-reinforcement involving standard-setting and self-evaluation ("Good, I'm doing fine"); and (d) coping skills and error-correcting op-

> tions ("That's okay . . even if I make an error, I can go slowly"). Such cognitive training is conducted across tasks, settings, and people in order to ensure that children do not develop task-specific response sets, but, instead, develop generalized strategems. [Meichenbaum and Asarnow 1979, pp. 15–16]

While the preliminary results of the few intervention studies employing cognitive strategies are promising, most of the empirical and clinical work applying cognitive strategies with deviant adult and child populations has yielded meager generalized outcomes (Ledwidge 1978; Denicola 1979; Meichenbaum and Asarnow 1979). Self-instructional and -evaluative training with schizophrenics has been disappointing. Most clinicians have reported that patients appear bored, fail to attend to or get involved with the training procedures, and do not reliably carry out assignments to practice the self-control skills outside of the training sessions. To improve the results of cognitive training, investigators teaching problem-solving strategies to retarded clients have recommended alterations in the training procedures, including: (1) greater duration of training; (2) rationales for the purpose and usefulness of cognitive strategies; (3) fading of prompts and modeling from the trainer; (4) increased demand for and monitoring of mental involvement in the tasks; and (5) training across settings, problems, and persons. Since some of these recommendations have been incorporated into the Camarillo/UCLA social skills training program, the full report of the results and followup data from this program will serve as a further test of the utility of teaching cognitive and problem-solving skills to schizophrenics.

There are suggestions from the experimental psychopathology literature that additional tactics might be helpful in improving the learning of social skills by schizophrenics. These include such procedures as prominent posting of graphics that prompt patients to follow training procedures; monitoring levels of arousal and "information overload" through psychophysiological and cognitive tests; repeated practice and overlearning; and allowing patients to temporarily "escape" or take a "timeout" from training when it becomes overstimulating. It would also be desirable for social skills assessors and trainers to recognize the diversity in the cognitive and attentional deficits and problems that schizophrenics demonstrate. This will require a more personalized clinical approach that takes into account each individual's cognitive deficits, assets, and needs.

Assessing the cognitive level in outcome studies may become an even more important feature of clinical research as investigators begin to conduct preventive intervention with children and adolescents who are considered to be at risk for developing schizophrenia. The underlying genetically transmitted vulnerabilities to schizophrenia are, in part, manifested by deficits in attention and information-processing (Asarnow, in press; Asarnow et al. 1978). Hence, preventive strategies may target change in these cognitive levels as more primary intervention targets that will, if improved, lead to a "ripple effect" with consequent improvement in the social, vocational, community, symptomatic, and familial spheres.

Similarly in the adult schizophrenic, when neuroleptic drug therapy leads to improvements in symptomatic status, it is likely that the drug is only indirectly affecting symptoms. The primary locus of drug effects is probably at basic neuropsychological mechanisms that mediate attention and information-processing functions. The adult schizophrenic who shows distractibility on the job, and withdrawal from family and friends after discontinuing neuroleptic medication, may have experienced cognitive deficits as a first stage of decompensation. Thus, use of methods for measuring cognitive functioning may eventually enable clinicians to detect the "early warning signals" of schizophrenic relapse and to engage in more timely secondary prevention efforts.

Summary

This review of the various methods of assessing social skills suggests that schizophrenics' characteristic cognitive and motivational deficits have an impact on social skills assessment and training outcomes. The methods of assessing social skills are varied, indeed; there are wide differences in the definitions of the construct "social skills," with resultant differences in the quality and quantity of assessment information. Questions of the reliability and validity of these techniques have only recently been addressed, and the results indicate that further attention must be paid to improving the psychometric qualities of these methods. The relationships among social skills, psychopathology, family interactions, vocational skills, and basic cognitive and motivational deficits have yet to be explored. These relationships among the multiple dimensions of behavior change are likely to yield important data for developing better assessment and treatment techniques.

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Social Dysfunction and Treatment Failure in Schizophrenia

by Carmi Schooler and Herbert E. Spohn

Abstract

Recent evaluation of a 20-year-old experimental ward resocialization program for chronic schizophrenics indicates that the general level of activity, much of it social, was disruptive to the psychological functioning of patients, particularly sicker ones. Antipsychotic drugs positively affected psychological functioning and also decreased social behavior. A review of other studies indicates that we are not unique in finding that intensive socioenvironmental therapies have adverse effects on schizophrenics. Furthermore, a wide range of studies indicates that schizophrenics are prone to avoid social interaction and show a decrement in functioning as the intensity of such interactions increases. Unfortunately, although various hypotheses seem feasible, little is known about the reasons for schizophrenics' social dysfunction and little research is presently being done. Given the recent findings that neuroleptic drug treatment by itself is insufficient to keep many patients out of the hospital and that those that stay in the community show an increase in withdrawal, the development of successful treatment programs for schizophrenia may hinge upon our learning more about the nature of and reasons for the schizophrenic's social dysfunction.

This article reports an experimental treatment failure that took place 20 years ago. Our general finding is that the chronic schizophrenic patients on a resocialization-oriented experimental ward ended our program in worse psychological condition than patients on the custodially oriented control ward.

Although we believe the evaluation, design, and measurement of this program are reasonable by contemporary standards and the approach and its rationale carefully documented, the report of such an "ancient" failure would be of no more than historical interest and cathartic value if it did not add something to our present knowledge. One value such findings have is that they serve as a vantage point for reviewing subsequent research by showing how, if we had known then what we know now, we would not have been so bitterly surprised and disappointed. These data, however, can do more than serve as a focus for a literature review. Both their quality and the emergence of new statistical techniques make it possible to use these data to add meaningfully to what we now know.

The Pretreatment Ward Setting

In 1956 when planning for the experimental milieu treatment started, medication was just beginning to come into use, but the liberalizing spirit that subsequently pervaded the mental hospital world was in no way manifest at the large Veterans Administration hospital at which our work was done. Well over 60 percent of the patient population of this hospital

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were chronic schizophrenics. Mental patients who were susceptible to social rehabilitation by means then available had been discharged years before. Besides the occasional use of the new antipsychotic drugs, treatment of chronic schizophrenics under this regimen consisted largely of the busy-work adjunctive therapies. Discharge rates were low, readmission rates high. A heavy aura of pessimism pervaded, and personnel at all levels regarded as futile any concerted treatment efforts. Preoccupation with administrative detail and very tight control over patient movement and initiative served to limit any contact with patients that might lead to what was widely regarded as inevitably painful and disappointing therapeutic involvement.

In this context, we came to regard the chronic schizophrenic patient as a socially disengaged, anomic individual, who purposefully avoided interpersonal engagement and preferred the impoverished and undemanding role that the institution assigned to him. The institution, in turn, imposed no sanction upon the expression of pathological or abnormal behavior which did not interfere with the smooth functioning of ward routine. Thus, the interpersonal environment of the ward provided no opportunity for reality testing and the discovery of the social inutility of inappropriate behavior.

The hospital's view of the chronic schizophrenic as incompetent and unable to take any rational initiative on his own behalf was made manifest in the form of an extreme control of every aspect of the patient's life, which cast him in the role of a total dependent. This implied not only that a variety of choices, normally made by individuals for themselves, were made for chronic schizophrenic patients by hospital personnel but also, and more significantly, that the community of patients on the ward was thus no community at all. There were no common purposes achievable through cooperative or competitive enterprise, there was no pattern of role differentiation and, of course, no extended social interaction. The ward in this hospital setting was primarily an aggregate of isolates (Schooler and Spohn 1960*a*).

We came to believe that the pattern of asocial and inappropriate behavior of hospitalized chronic schizophrenics resulted from an interaction between institutional processes on the one hand and disease processes on the other. It seemed to us that the schizophrenic's need for social withdrawal, self-isolation, self-effacement, and restriction of his life space was sometimes subtly, sometimes overtly fostered and abetted by the institution. Consciously or unconsciously, these patient orientations were used by the hospital staff to make the patient into a tractable hospital citizen who fitted smoothly and efficiently into a network of administrative and management routines predicated on the assumption of his incurability.

Such insights and feelings guided the development and implementation of an experimental "socioenvironmental" treatment program at the ward level.

Changes on the Experimental Ward

Major changes in the social, administrative, and physical structure were implemented on the 48-patient experimental ward. The total ward group was subdivided into five six-man and two nine-man groups. A "group leader," usually a psychiatric aide, but in some cases an adjunctive therapist, was permanently assigned to each group. These leaders met with their groups twice a day, 5 days a week, in permanently assigned group meeting rooms or alcoves. Group leaders were trained to encourage discussion among patients about attitudes and feelings they shared concerning events in and outside the hospital. They were also trained to promote feelings of group participation and belonging and to foster the view that the group was a small social unit which both satisfied individual needs and made demands for individual contributions to group welfare.

In order to achieve these aims through the group meetings process, group leaders employed a number of procedures. They sought to stimulate group discussion of current events. Individual patients were asked to read news stories out loud and others were encouraged to comment on them. Similarly, individual group members described projects undertaken in occupational therapy and were urged to comment on those of other patients in the group. Games entailing cooperative and competitive behavior were widely used by group leaders to stimulate and sustain social interaction. Patients who anticipated family visits were encouraged to share their feelings in this regard with the group both before and after such visits. Groups went on trips together to athletic games, to theaters and for shopping and were escorted on such trips by their group leader. Afterwards the group was encouraged to discuss the trip experience.

Finally the group leaders were trained to function as models and guides in reality testing, emphasizing, especially in the context of the group situation, the importance of controlling symptomatology in the interest of clear communication and group participation. Levels of group discussion and activity were carefully adjusted to the capacities of each group. In order to associate as closely as possible with the group experience those gratifications which remain important to chronic schizophrenics, group leaders distributed patient luxuries (mostly cigarettes) before one of the group experience periods, while before the second, they supervised a snack period with beverages and food. Typically, individual patients were encouraged to participate in the process of dispensing luxuries and comestibles to the members of their group. In order to extend the activity of the group beyond these sessions and to provide as many group-shared experiences as possible, the major ward activities—cleanup, shaving, showering, and eating—were reorganized as group functions.

Parallel with the small group structure, a program of intensified individually oriented activity was instituted. After a careful review of individual needs and capacities, off-ward therapeutic activity assignments were made for many patients, while the most withdrawn and confused patients received daily periods of occupational therapy and recreational activity. All patients were encouraged to avail themselves of increased opportunities to exercise individual choice in matters of food, personal care, clothing, luxuries, and participation in recreational activities. The formerly white and beige color scheme of the walls and the dormitory beds was broken by a variety of drapes, colored bedspreads, and pictures, in part selected by the patients themselves.

The group leaders were supervised by the ward nurse and ward psychologist at regularly scheduled semiweekly conferences. During both the training period and the supervisory conferences, emphasis was placed on the belief that the chronic withdrawal and alienation of the schizophrenic patient could be reversed through the intensification of interpersonal relationships. It was stressed that attention to individual needs and capacities would restore feelings of identity, self-confidence, and initiative, and that the example and guidance of group leaders would lead to the development of ward standards of behavior similar to those of a normal human community. As the implementation of the group process progressed, supervisory conferences began to take on increasing importance for group leaders. In such conferences they were helped to share and come to terms with feelings of frustration, resentment, and guilt in response to the difficulties they encountered in efforts to promote social interaction among the patients in their groups.

Methods of Measurement and Evaluation

Measurement. The 100 male veteran patients selected for this study were randomly assigned to two closed wards, one experimental, one control. The selection criteria were primary diagnosis of schizophrenia, 3 or more years of hospitalization, a stable adjustment on a closed ward, and poor prognosis for recovery. The patient groups thus selected had been continuously hospitalized for an average number of 8 years, with an average age of 42.7 years. Every major subdiagnostic category was represented in balanced numbers on both wards.

Baseline measures were collected for a period of more than a year, while the two wards continued to function under psychiatric, nursing, and administrative procedures in every way similar to those of the rest of the hospital.

Evaluations were focused on two concepts—social behavior and psychological functioning.

The measures of social behavior included:

- Percentage of observations of individual patients when engaged in social interaction. The Location Activity Inventory (LAI) (Hunter, Schooler, and Spohn 1962; Schooler and Parkel 1966) is a structured observational technique that gathers minimally inferential profiles of patients' location and activity patterns on a time-sampling bases.
- Rate of interaction with others. The Interaction Protocol (IP) (Solomon and Spohn 1958; Wilensky and Solomon 1960) is a prestructured observation instrument designed to assess the characteristics of patients' social inter-

actions on the ward. During each evaluation period, 55 one-hour periods of observation were made at random times during the day. The interaction rate is the ratio of the number of a patient's social contacts to the number of observation periods in which he was on the ward.

- Rate of interaction specifically with other patients (IP).
- Number of interactions initiated toward other patients (IP).
- Number of interactions initiated toward staff (IP).
- Number of interactions received from other patients (IP).
- Number of interactions received from staff (IP).

The measures of psychological functioning included:

- An abbreviated Wechsler Adult Intelligence Scale (WAIS). The subtests used include information, Digit Span, Picture Completion, Block Completion, Block Design, and Digit Symbol (Wilensky and Solomon 1960).[1]
- Rorschach Developmental Level Score (Becker 1956). This score is based on a one-response-per-card Rorschach in which a high score is interpreted as indicating a high level of perceptual organization and by inference a mature level of personality integration.
- Goodrich Psychiatric Rating Score (Goodrich 1953). Evaluation is based on a written report of a standard mental status exam conducted by psychiatric residents under staff supervision.
- Mental Health Rating Scale. A six-level global rating (made by the ward psychologist) is focused on the patient's presumed ability to assume independent responsibility in caring for himself.
- Nonfunctional behavior on the LAI (Hunter, Schooler, and Spohn 1962). Included are nonfunctional movement and object manipulation, nonsocial verbal, gestural and laughing behavior.

The measures used during the baseline period to examine patient adjustment were readministered on both wards after the experimental program had been in operation for 2 years. During this period the control ward remained under the standard regimen used by the hospital to treat chronic schizophrenics. At this time, 41 members of the experimental group and 34 of the control group were still on their respective wards.

Among the patients who remained in the study through the posttreatment measurement period, there were two significant differences in baseline measures, both of them on social variables, between the two wards. Among these patients there were significant differences in rate of interaction ($p = .021$) and rate of patient-patient interaction ($p = .037$). In both cases the patients who remained on the control ward showed a higher level of interaction than those who stayed on the experimental ward. As will be seen, the direction of this difference runs counter to the experimental effect which resulted in an increase in social behavior on the experimental ward.

Examination of the baseline observational data mirrored our bleak impressionistic picture of life on the wards. Patients spent less than 3 percent of their time in any kind of social interaction, and about 19 percent in nonfunctional pathological behavior. (For a more extensive description, see Hunter, Schooler, and Spohn 1962).

Given both the nature of the population and of several of the individual measures of social behavior and psychological functioning, the question of the reliability of the measurement of these two concepts arises. Test-retest studies such as this are particularly susceptible to the eventuality of measurement error because the magnitude of the effect of the pretreatment (independent) variables on the posttreatment (dependent) variables will be underestimated in direct proportion to the amount of error in the measurement of the pretreatment variables (Blalock 1972; Heise 1975).

Fortunately, Linear Structural Equations System Analysis (LISREL) makes it possible to obtain a measurement-error-free measure of a concept through the use of confirmatory factor analysis (Joreskog 1973; Maruyama and McGarvey 1980; Schooler, in press). Given multiple indicators of a concept, models can be constructed which divide the variance of each of the indicators into two parts—one part reflecting the concept being measured, the second part reflecting anything else, which for measurement purposes is considered error. Such models can take into account the possibility that errors of measurement are correlated over time—that whatever errors there may have been in the measurement of any of the indices of a concept in the pretreatment period are correlated with errors in the measurement of that index in the posttreatment period. The program reduces these models to a series of simultaneous equations, which it solves using iterative function minimization procedures. It also tests the significance of the loadings of the indices on the concepts and the degree of fit of the model to the original data.

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[1] Some IQ data were missing for 26 subjects. Estimates of these scores were made by using the other variables in the model to predict IQ and using the resultant constants and beta weights to construct estimated scores.

The measurement models for both social behavior and psychological functioning seem to reflect their respective underlying concepts and to fit the original data quite well.[2] Examination of the measurement models for social behavior (see table 1) indicates that there was a shift between the pretreatment and the posttreatment concepts in the relative importance of the different indicators of social behavior. Initiating interactions and interacting with peers were more reliable indices of social behavior during the posttreatment than the pretreatment period. In the pretreatment period the LAI measure of social activity, which does not specify the initiator or the other participants, had the highest loading while in the posttreatment period it had the lowest. Receiving social interactions from the staff, which had the second lowest loading on the posttreatment measure, also had a higher loading on the pretreatment measure. Receiving interactions from other patients had a similarly higher loading on the pretreatment than the posttreatment measure. On the other hand, rate of patient-patient interactions, which had the lowest loading on the pretreatment measure, had the second highest loading on the posttreatment measure and initiating interactions with other patients had the highest. This pattern of different loadings suggests that social behavior was more reliably measured by indices reflecting passive social behavior during the pretreatment and indices reflecting active social behavior during the posttreatment. Despite these differences both pretreatment and posttreatment

Table 1. Measurement model for social behavior

Indicator	Standardized loading on pretreatment social behavior factor	Standardized loading on posttreatment social behavior factor	Standardized over-time correlated error
Percent social behavior (LAI)	.89	.38	(−.005)
Rate of interaction (IP)	.35	.61	(−.006)
Rate of interaction with patients (IP)	.26	.94	(−.01)
Interactions initiated toward patients (IP)	.82	.95	(−.01)
Interactions initiated toward staff (IP)	.76	.77	.16
Interactions received from patients (IP)	.70	.61	(.10)
Interactions received from staff (IP)	.57	.39	.49

Chi-squared/*df* = 4.8950; () indicates NS, $p > .05$.

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[2] The confirmatory factor analyses of the measurement models were carried out using the MILS program, an advanced version of LISREL (Joreskog and van Thillo 1972) developed by Ronald Schoenberg. The correlations between the confirmatory factor analysis based concepts and other concepts used in the causal analyses were obtained through the use of factor scores based on Bartlett's method (Lawley and Maxwell 1971, pp. 109–112). MILS not only provides factor weights for deriving such scores but also makes possible an estimate of their reliability by producing their correlations with the true scores. The correlations between these factor scores and the other variables were then computed and the resulting correlations corrected for the known unreliability of the Bartlett factor scores.

measures unquestionably index patient social behavior.

Examination of the measurement model for psychological functioning indicates that the loadings of the different indices are remarkably similar for both periods (see table 2). Level of intellectual functioning as measured by the abbreviated WAIS has the highest loading at both times, and the other loadings, including the one based on ward observations (LAI nonfunctional), are reasonably high and significant.[3]

Evaluation. Two types of statistical analysis were carried out to examine the effectiveness of the ward program. The first is an analysis of covariance comparing the posttreatment means of the experimental and control wards adjusted for pretreatment level. This analysis is performed on each of the 12 variables used as indicators of the psychological and social measurement models (contained in tables 1 and 2).

However, such an analysis cannot readily be carried out when the factor scores based on the measurement models are adjusted for measurement error, since the resultant output is a variance-covariance matrix among the relevant variables. Such a matrix can, however, be used for reduced form equation analysis, the second type of analysis presented, which simply consists of a set of multiple regression analyses in which each dependent variable is allowed to be affected by the complete set of independent variables. Besides making it possible to adjust for the effects of measurement error, such an analysis has several additional advantages.[4] It is very similar to analysis of variance when the latter is reduced to its basic regression components. The standardized reduced form coefficients (which are the paths cited in the text) tell how much change can be expected in the dependent variable per unit change in the independent variable.

The dependent variables in the reduced forms equation analysis are (1) posttreatment psychological functioning; (2) posttreatment social behavior. The independent variables are (1) experimental condition (experimental ward = 1, control ward = 0); (2) pretreatment psychological functioning; (3) pretreatment social behavior; (4) age; (5) number of weeks on antipsychotic drugs;[5] (6) the residualized orthogonal interaction of experimental condition and pretreatment psychological functioning;[6] and (7) the residualized

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[3] Although there were some significant differences in the individual indices, there was no significant difference between the two wards in the social behavior factor among the patients who remained in the study through the posttreatment measurement phase. There was, however, a significant difference ($p = .05$) on the psychological functioning factor. The subjects who stayed on the experimental ward had a higher level of pretreatment functioning than those who remained on the control ward, a difference which runs counter to the experimental effect.

[4] Since every independent variable is allowed to affect every dependent variable, such an analysis should not be confused with a confirmatory causal analysis, in which the paths from some of the independent to some of the dependent variables may be hypothesized not to exist. Several more complex forms of causal analysis were tried in an attempt to confirm hypotheses about reciprocal causal effects among the posttreatment measures, but relatively parsimonious reduced form equation analysis provides the clearest and least ambiguous results.

[5] The two drugs used were reserpine and chlorpromazine. Unfortunately, this is the only measure of chemotherapy recoverable. Among the patients who stayed through the posttreatment measurement, there were no significant differences between the two wards in average percent weeks on medication (control ward = 71 percent, experimental ward = 78 percent, $p = .47$).

[6] Residualized interaction terms orthogonal to the main effects whose interaction they represent had to be constructed because the inclusion of nonorthogonalized interaction terms in a regression equation would render meaningless the main effect estimates (Cohen 1978; Cohen and Cohen 1978). Briefly, the residualized interaction terms were developed by first constructing an "observed" interaction term. Subjects who were in the experimental group and above the sample median in social behavior were assigned the score they had obtained for social behavior while all other subjects were assigned a value of 0. This observed interaction term was then used as a dependent variable in a multiple regression equation in which the independent variables were experimental group and social behavior score. Estimated scores were then constructed on the basis of the constants and beta weights of the resultant regression equations and the estimated scores subtracted from the observed ones. When they are in this residual form, the interaction terms are uncorrelated with the main effects and they measure only that variance which is unexplained by the main effects.

Table 2. Measurement model for psychological functioning

Indicator	Standardized loading on pretreatment psychological functioning factor	Standardized loading on posttreatment psychological functioning factor	Standardized over-time correlated error
IQ (abbreviated WAIS)	.80	.78	.27
Developmental level (Rorschach)	.61	.49	.47
Goodrich Psychiatric Rating	.74	.73	(.09)
Montrose Mental Health Rating	.77	.67	(.06)
Percent nonfunctional behavior (LAI)	−.37	−.37	−.33

Chi-squared/df = 2.4651; () indicates NS, $p > .05$

orthogonal interaction of experimental condition and pretreatment level of social behavior.

Results

For the individual items that were the dependent variables in the covariance analyses, the differences between the experimental and control wards in the posttest means adjusted for initial level (but not measurement error) are not generally significant. However, the direction of the differences is congruent with the hypothesis that the experimental condition increased the level of social behavior and decreased the level of psychological functioning (see table 3). The only two exceptions are nonfunctional behavior, where there is no difference between the wards, and the mental health rating scale, on which the experimental ward did relatively better than the control ward. In evaluating the latter finding, it should be borne in mind that the global mental health ratings were not made blindly, but by the ward psychologist. In such circumstances raters' expectations may well produce results contrary to those obtained by more controlled evaluation procedures.

Comparison of the patterning of the control and experimental group posttreatment adjusted means for social behavior shown in table 3 reveals something about both the quantitative differences and the qualitative differences between the two groups. Thus the experimental ward group is seen not only as socially more active at posttreatment and as receiving a much greater number of social overtures from staff, but they also show a trend toward initiating a larger number of interactions vis-à-vis both staff and other patients than the control group. This implies some reduction in the experimental ward group in social passivity characteristic of chronic schizophrenic patients (such as the control group) on custodially oriented wards in public mental hospitals in the era in which this study was performed.

Examination of the reduced form equation analysis, in which the effects of measurement error have been purged from the psychological and social measures, reveals that the level of stability from pretreatment to posttreatment of both psychological and social functioning is very high (see table 4). The standardized reduced form coefficient from pretreatment to postreatment psychological functioning is .92, and from pretreatment social behavior to posttreatment social behavior .92. Since we never expected any miracles, we were not surprised by the high stability of the patients' social and psychological functioning. What we were not originally prepared for is the negative effect on the patients' psychological functioning of being on the experimental ward. The path from being in the experimental condition to posttreatment psychological functioning is −.20. Furthermore, this decrement in the experimental ward patients' psychological func-

Table 3. Analysis of covariance of individual posttreatment measures covarying pretreatment level

Variable	Adjusted means		F	p
	Control	Experimental		
Social behavior indicators				
Percent of social interaction (LAI)	.03	.07	8.683	.004
Rate of interaction with others (IP)	.37	.46	.055	.815
Rate of interaction with patients (IP)	.13	.19	.496	.484
Number of interactions initiated toward patients (IP)	6.04	7.21	.506	.479
Number of interactions initiated toward staff (IP)	4.12	7.87	1.791	.185
Number of interactions received from patients (IP)	6.59	9.00	2.734	.103
Number of interactions received from staff (IP)	6.53	14.63	39.235	.000
Psychological functioning indicators				
Abbreviated WAIS	81.08	76.31	.551	.460
Rorschach developmental level score	26.38	22.26	1.991	.166
Goodrich Psychiatric Rating score	2.48	2.20	.563	.128
Mental Health Rating Scale	31.65	36.08	9.577	.003
Nonfunctional behavior (LAI)	.13	.13	1.358	.248

tioning took place in a context of increased social interaction. The path of .13 from experimental condition to posttreatment social functioning indicates that the experimental manipulations did succeed in increasing the level of the patients' social behavior compared to that on the control ward.

An anecdote may serve to dramatize our finding that as social interaction on the experimental ward increased, the level of psychological functioning decreased. A patient on the experimental ward described his preexperimental ward program self-isolation and withdrawal as akin to being inside a glass shell from which he could see out but could not hear what was going on around him. With the advent of the program, he experienced both staff and other patients as seeking to shatter his shell and this frightened him greatly. Such a reaction seems to have been more prevalent among the sicker than the healthier patients on the experimental ward.

While the significant main effect for ward indicates that being on the experimental ward resulted in poorer psychological functioning, the significant residualized interaction effect (path = .14) of ward and initial psychological level indicates that this effect is stronger for patients whose initial level of psychological functioning was lower. Thus the sicker patients on the experimental ward were relatively more adversely affected than were the healthier ones.

In this sample of chronic schizophrenics, age, not surprisingly, is

Table 4. Significant standardized reduced form coefficients[1]

		Posttreatment	
		Psychological functioning	Social behavior
1.	Experimental ward	−.20	.13
2.	Pretrial psychological functioning	.92	
3.	Pretrial social behavior		.92
4.	Interaction ward × pretrial psychological functioning (residualized)	.14	
5.	Age	−.10	−.18
6.	Antipsychotic medication	.13	−.08

[1] Indicate the amount of change in standard units that can be expected in a dependent variable per unit change in an independent variable with the effects of the other independent variables controlled.

related to low levels of both social behavior and psychological functioning in the posttreatment period. The path from age to posttreatment social behavior is −.18 and to posttreatment psychological functioning −.10.

Initially more surprising, but more in line with the findings on the negative effects of the experimental ward on psychological functioning, are the negative effects of antipsychotic medication on social behavior. The path from number of weeks on antipsychotic drugs to posttreatment social behavior is −.08. At the same time, the path from weeks on medication to posttreatment level of psychological functioning is moderately strong and positive (.13).

The pattern of results strongly suggests that the general level of activity on the experimental ward, much of it social, is disruptive to the psychological functioning of the patients, particularly the sicker ones. In this situation medication decreases the amount of social behavior and possibly blunts its effects.

Finally, our evidence suggests that our intensive socioenvironmental treatment effort did not repay its cost to patients by preparing them for life outside of the hospital. There were no significant differences between the experimental and control groups in discharge or length of stay in the community during a period following termination of the project from May 1960 to September 1965. That the proportion of experimental ward patients (25 percent) discharged in the first 3 years after termination of the program was slightly larger than that of control ward patients (9 percent) is probably due to the fact that experimental ward patients were better known to staff than control ward patients.

Discussion

The results described above are obviously most applicable to long-term, chronic, male, veteran schizophrenics subjected to a particular treatment regimen in the late 1950s. There may well be a declining gradient of generalization to the extent that the nature of the social situation or of the schizophrenic population differs. However, an examination of the literature indicates that congruent findings have generally emerged among a wide range of schizophrenic populations and social contexts. Thus more recent studies indicate that we were not unique in finding that intensive socioenvironmental therapies have an adverse effect on the psychological functioning of hospitalized schizophrenics. In a review article Hemsley (1978) cites a series of reports of deterioration in the behavior of at least a minority of schizophrenics in intensive rehabilitation programs. He also finds evidence of increased behavioral abnormality among schizophrenics who took part in token economy programs.

Reviewing his own and related work, Wing (1975) concludes:

> negative impairments [e.g., social withdrawal, flatness of affect, and lack of motivation] occur more frequently and more intensely in conditions of social poverty. . . . Florid relapse [unpredictable associations, incoherence of speech, hallucinations] occurs more frequently and intensely in socially overstimulating environments . . . through too vigorous attempts at rehabilitation or too intensive group therapy. [p. 257]

In another review article Van Putten and May (1976) conclude "that milieu therapy does not add much to the treatment of schizophrenics once adequate chemotherapy is used and gross neglect corrected" (p. 230). They cite a series of treatment studies supporting "the concept that the application of intensive milieu therapy is conceptually unsound for some schizophrenic patients" (p. 233). They also discuss three studies (Hamilton et al. 1960;

Freedman et al. 1961; Paul et al. 1972) in which drug treatment seems to increase social withdrawal and to decrease both social responsiveness and the effectiveness of social interventions. These latter results are intriguing from the vantage point of our finding that chemotherapy has a positive effect on psychological functioning and a negative effect on social interaction.

Also relevant are the ward studies carried out by Kellam et al. (1966, 1967) on the effects of ward atmosphere on the psychological functioning of schizophrenics on admission wards. In these studies which were conducted as part of a larger study on the effects of phenothiazines, ward atmosphere was characterized in terms of a series of dimensions measured by staff report or observation. Among these dimensions are disturbed behavior (divided into aggressive and bizarre) and adult status (a measure of the degree to which patients on wards are allowed to maintain basic symbols of adulthood). The first of these studies reports a correlation of .43 between the ward characteristics of aggressive behavior and staff patient contact. Although some of this correlation may be due to the staff's response to the patients' aggressive behavior, it is also possible that some of the patients' aggressive behavior may be a reaction to the staff's social intrusiveness. The second article presents results which the authors find paradoxical. Although, as they predicted, ward atmospheres characterized by disturbed behavior seemed to lead to greater symptomatology, contrary to their expectations, so did ward atmospheres which allocated the patients more adult status. What both of these characteristics may have in common is greater social intrusiveness. Other patients' aggressive and bizarre behavior can be as intrusive as the social demands implied by treating the patient as an adult. Interestingly, in terms of the hypothesis that antipsychotic drugs act to dampen the effects of social intrusion, the effects of these two ward characteristics are greater for patients receiving placebo than for those receiving drugs.[7]

The adverse effect of intensive socioenvironmental therapy programs is not limited to hospitalized schizophrenics. Goldberg et al. (1977) found that symptomatic schizophrenic patients in the community relapsed more quickly when they received Major Role Therapy (a combination of social casework and vocational rehabilitation) than when they did not. The results of this study are also similar to ours (and in keeping with those of Fairweather et al. 1960) in that a significant interaction was found, indicating that the more symptomatic patients were more likely to be adversely affected by the social intervention.

The negative effects of socioenvironmental treatment programs become less surprising when we consider the evidence that schizophrenics are more likely than others both to avoid social contacts and to show a decrement of psychological functioning as social situations become more intense.

Examination of both their actual behavior and their expressed preferences indicates that schizophrenics are more prone to avoid social interaction than are others in similar situations. Thus the only significant behavioral difference between hospitalized schizophrenics and other chronic psychiatric patients observed in an LAI study of randomly selected patients in a large mental hospital is that the schizophrenics engage in less verbal social behavior (Schooler and Parkel 1966). In the same study the schizophrenic patients rated themselves as significantly more likely to inhibit the expression of interpersonal emotion than did the other patients. In another study, schizophrenics were found to express a distinct preference, compared to normals, for reducing the degree of interpersonal interrelatedness in a two-person task situation or, if possible, for doing the task alone (Schooler 1963).

That such a preference for social withdrawal is not an ephemeral problem is suggested by an analysis limited to "behavior anteceding the first manifestation of psychotic onset" (Gittelman-Klein and Klein 1969, p. 39). The results show that "withdrawn asocial behavior, and a lack of interest in activities involving one's peers are uniformly associated with decreased frequency of successful, lasting recovery" (Gittelman-Klein and Klein 1969, p. 44).

Both experimental and nonexperimental evidence also indicate that increasing the intensity of schizophrenics' social interactions may result in a decrement in their psychological functioning. An experiment by Hunter (1960) demonstrated that the level of task performance of chronic schizophrenics decreases as a function of their interdependence with their task partners. Johannsen (1961) showed that schizophrenics perform at a significantly lower level with social than with nonsocial reinforcement. Schooler and Spohn (1960*b*) found that experimentally increasing group pressure disrupts the performance of chronic patients more than it does that of normal controls.

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[7] Analyses were also performed for three ward atmosphere measures of social contact: aloneness, cluster-size, and staff-patient contact. The most frequent significant findings were for cluster size. Unfortunately, the social implications of this variable are unclear. It is indexed by "the average number of patients present per social occasion." A high number may well mean that the social interaction that does take place is less individualized and intense.

Examining schizophrenics' adjustment in the community, Vaughn and Leff (1976), replicating an earlier study by Brown, Birley, and Wing (1972), found that contact with a relative who expresses a high degree of emotion is significantly associated with a high relapse rate of schizophrenics. Furthermore, although maintenance therapy with phenothiazines partially ameliorates the negative effect of extensive contact with an emotionally expressive relative, the negative effects of such interpersonal contact are also seen among patients receiving these drugs.

The reasons for the deleterious effects of social interaction on schizophrenics remain in question. Given the present state of our knowledge, many plausible and not necessarily contradictory hypotheses can be put forth. The problem may be primarily a cognitive one. Social interactions are generally cognitively complex. Hemsley (1977), among others, has argued that schizophrenics may be in a state of information overload. As a possible protection against such an overload, acute schizophrenics tend to adopt a perceptual style which reduces the perceived intensity of stimuli (Schooler et al. 1976). Chronic schizophrenics, who reduce the perceived intensity of stimuli less than do acutes, may protect themselves from cognitive overload by reducing their social contacts further.

There are also noncognitive reasons why schizophrenics may be negatively affected by social interaction. Besides being a cognitively complex object, another person is also likely to be a source or target of emotion. Schizophrenics may have particular difficulties in giving or receiving positive or negative emotion (Fromm-Reichmann 1950; Schooler 1963). Nor can psychodynamic explanations not related to emotional difficulties be ruled out. Thus it is possible, as Fromm-Reichmann (1952) has suggested, that interpersonal "closeness increases the schizophrenic's ever-existing fear of . . . losing his identity, of losing the sense of the boundaries between himself and the outside world" (p. 105).

In any case, the evidence is preponderantly in the direction of higher autonomic arousal for schizophrenics (Zahn, Carpenter, and McGlashan 1981) and the added arousal coming, for whatever reason, from interpersonal interaction may be dysfunctional. The possibility that highly aroused patients may therefore avoid social contact is suggested by Venables and Wing's (1962) finding that for all but coherent deluded schizophrenics, withdrawal is highly related to arousal. Moreover, in chronic schizophrenics phenothiazines somewhat reduce excessive levels of arousal (Spohn et al. 1977). It may be, therefore, that medicated patients can, as noted above, tolerate social interaction somewhat longer than nonmedicated patients.

Schizophrenics differ not only in the level but also in the pattern of their arousal. The schizophrenic's arousal pattern shows less specific responses to environmental demands (Zahn, Carpenter, and McGlashan 1981), and even among schizophrenics specific responses are linked to better performance. Being in a social situation may affect the schizophrenics' ability to fit their responses to the situational requirements. Experimental evidence suggests that "the social nature of the situation can affect the direction of the relationship between arousal and performance" (Schooler and Zahn 1968, p. 400).

A cursory examination of the reference list for the present article quickly reveals that most of the studies specifically directed at examining the schizophrenic's social functioning are not particularly new. Perhaps in part because of the search for an underlying biochemical cause and the apparent efficacy of the psychotherapeutic drugs, there have been few recent studies concerned with either the causes or the therapeutic implications of the schizophrenic's social dysfunction.

Findings from a recent study by N.R. Schooler et al. (1979) should serve to revive concern with these problems. In their study of the comparative effectiveness of injectable depot fluphenazine decanoate or oral fluphenazine hydrochloride, 28 percent of the patients relapsed within their first year of community treatment.

Contrary to the original hypothesis, there were no significant differences between the two treatments, thus ruling out the widely held belief that phenothiazine treatment failures are primarily due to patient noncompliance in taking their oral medication. Instead the evidence suggests that phenothiazines by themselves do not necessarily permit schizophrenics to function at a level which will permit them to stay in the community.

Even more pertinent to the results of our socioenvironmental treatment study is the finding that the symptoms of emotional withdrawal and blunted affect were actually more prevalent among nonrelapsed patients at the end of the 1-year community maintenance phase than they were in the beginning, although the prevalence of all other symptoms had decreased. Thus it would appear that some level of social withdrawal and noninvolvement is functional for the schizophrenics' adjustment to their social environment. It should be remembered that in our study not only did psychotherapeutic medication increase level of psychological functioning, it also decreased social behavior. We are, however, left with a difficult conundrum. On the one hand, the N.R. Schooler et al. study demonstrates that medication by itself is not sufficient to keep many schizophrenics adjusted at a level acceptable to the community. On the other hand, socially based attempts at improving the schizophrenics' adjustment seem to founder on the schizophrenics' apparent need to avoid social interaction and apparent disturbance in psychological functioning when they cannot do so. The development of successful treatment programs for schizophrenia may hinge upon our learning more about the nature of this social dysfunction.

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Outcome in Schizophrenic and Similar Paranoid Psychoses

by Hans-Jürgen Möller, Detlev von Zerssen, K. Werner-Eilert, and M. Wüschner-Stockheim

Abstract

A 5-year followup study of patients with schizophrenic or paranoid psychoses was performed using standardized instruments. Less than half of the patients had a poor global outcome. Several findings from other recent outcome studies were replicated. Besides data on occupational history and psychiatric hospitalization, psychopathological characteristics assessed at discharge by psychiatrists' ratings and patients' self-ratings proved to have predictive value.

A large number of studies investigating the outcome of schizophrenia have been carried out. Although these studies have generated many hypotheses about variables that are important predictors of outcome, methodological shortcomings have limited confidence in their findings. Most studies used retrospective evaluation techniques or nonstandardized instruments which may have introduced significant bias. Some more recent studies, however, have avoided such methodological problems by studying patients prospectively. Unfortunately, these excellent studies have evaluated patients over short periods of time, generally from 1 to 2 years (e.g., Schooler et al. 1967; Astrachan et al. 1974; Hogarty et al. 1974; Strauss and Carpenter 1974; Wittenborn, McDonald, and Maurer 1977; World Health Organization 1979). Only the 5-year followup study of patients in the International Pilot Study of Schizophrenia (IPSS) covers a longer time period. Thus far, data from this 5-year followup study have only been published by the Washington field center of the IPSS (Hawk, Carpenter, and Strauss 1975; Strauss and Carpenter 1977). Because we have also carried out a 5-year followup study, using standardized instruments and documenting similar variables, we decided to compare our results (Möller et al. 1981*a*, *b*, in press *a*, *b*) with the 2-year (Strauss and Carpenter 1974; World Health Organization 1979) and 5-year (Hawk, Carpenter, and Strauss 1975; Strauss and Carpenter 1977) results of the IPSS followup.

Methods

Psychopathological characteristics of all psychiatric inpatients treated at the Max Planck Institute of Psychiatry (MPIP) are well documented through the use of standardized rating instruments (Barthelmes and von Zerssen 1978). For the followup investigation reported here, we selected 103 out of the 225 inpatients diagnosed as suffering from a schizophrenic[1] or paranoid psychosis who were admitted for treatment during 1972–74. The 103 patients met the following project criteria: availability of complete psychiatric documentation and residence in Munich or surrounding area at time of admission. This sample was representative of all 225 inpa-

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[1] Patients with schizoaffective psychoses (ICD 295.7) were excluded because recent studies suggest that they should be classified with affective psychoses.

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tients with regard to sex, marital status, diagnostic subgroup, and global psychopathological state at discharge.

At followup, 5–6 years after discharge, seven patients had died, five by suicide. Apart from self-ratings, complete followup data could be obtained from 78 patients. In three other cases, we received extensive information by interviewing relatives. These 81 patients were representative of the original sample with regard to sex, age, diagnostic subgroup, marital status, and global psychopathological state at discharge.

Seventy-seven percent of patients were diagnosed as schizophrenics (ICD 295) and 23 percent as suffering from other types of paranoid psychoses (ICD 297, 298.2, 298.3, 298.9). Diagnoses were made by ward psychiatrists using ICD criteria (World Health Organization 1978). Diagnoses were discussed in weekly conferences under the supervision of the Head of the Department (von Zerssen) or his representative (Mombour). Agreement between clinical and computer-derived diagnoses (DiaSiKa program; von Zerssen, in preparation) was very high—88 percent for the diagnosis of schizophrenia, for example.

Sixty percent of the patients had never previously been admitted to a psychiatric hospital. The sample was almost equally divided between men (49 percent) and women (51 percent). Sixty-six patients (82 percent) were 40 years old or younger, and only one patient was over age 60. Treatment consisted of neuroleptics (mostly haloperidol, in individualized but not high dosages) and sociotherapy. Hospitalization was no longer than 3 months for 92 percent of patients, with only 8 percent staying for more than 4 months. Usually 1 to 2 weeks before discharge, the oral neuroleptic medication was changed to an intramuscular depot neuroleptic.

Our sample is comparable to the schizophrenic population of university clinics, but not to that of county hospitals where chronic patients are overrepresented. It also appears comparable to the IPSS sample, which excluded chronic patients (with psychotic symptoms of more than 2 years' duration in the 5 years before index admission, or hospitalized more than 3 years).

The principal part of the study is prospective: psychopathological data were obtained on admission and discharge through the use of well-standardized instruments. A global rating of psychopathological state at discharge and sociodemographic data of several types were also routinely collected. Only the anamnestic data had to be gathered from records. At followup, the same instruments were used to assess psychopathology, and in addition, a differentiated rating of social adjustment was made. Psychopathological characteristics and social adjustment were rated not only by psychiatrists, but also by the patients themselves and their relatives. Thus, as has been recommended by a number of investigators, multiple outcome criteria (Keniston, Boltax, and Almond 1971; Strauss and Carpenter 1972) and sources of information (Baumann and Seidenstucker 1977; Seidenstucker and Baumann 1978) were used.

The following data sources were included:

- Inpatient Multidimensional Psychiatric Scale (IMPS; Lorr 1974)—filled out by psychiatrists; documents schizophrenic and depressive symptoms.
- Clinical Self-Rating Scales (KSbS; von Zerssen 1976)—filled out by patients; document depression, paranoid tendencies, and somatic complaints.
- Scales for Rating Social Adjustment (Wüschner-Stockheim, in preparation).
- Global Assessment Scale (GAS; Spitzer, Endicott, and Fleiss 1976)—measures global level of functioning.
- Sociodemographic information.
- Hospital records concerning premorbid adjustment, impairment of working ability during the year before index admission, personality change before index admission, onset characteristics, duration of occupational problems (inability to work or unemployment) during the 5 years before index admission.
- Followup data concerning employment problems, duration of psychiatric hospitalization, and duration of paranoid-hallucinatory symptoms during the followup period; impairment of working ability in the year before followup, personality change at followup, and global psychopathological state at followup.

Statistical Analysis. The frequency distribution of the global outcome criterion (GAS) was first calculated. To analyze the relationships among the different outcome criteria, product-moment correlations between the GAS score and the other variables were calculated. For these and the following calculations, only syndrome scores of the IMPS and the

KSbS were taken into account. For the IMPS, instead of the original 12 factors (Lorr 1974), five superfactors (von Zerssen and Cording 1978) were used. The ratio of amelioration of these scores was calculated using the following formula: score at admission minus score at discharge divided by score at admission. To evaluate the relationships between predictor and outcome variables, product-moment correlations were calculated between each potential predictor variable and several outcome criteria. Similar to the World Health Organization (1979) study, stepwise multiple regression analyses were performed to optimize the prognosis of global outcome by a combination of predictors. These analyses were performed for all predictor variables together (without self-rating data), for the IMPS data alone, and for the IMPS and KSbS data.

Table 1. Level of functioning (GAS score) at followup

	Information from			
	Patients[1]		Relatives[2]	
Level of functioning	No.	%	No.	%
100–91 No symptoms	8	10	5	10
90–81 Transient symptoms	8	10	0	0
80–71 Minimal symptoms	4	5	5	10
70–61 Some mild symptoms	14	18	11	23
60–51 Moderate symptoms	8	10	1	3
50–41 Any serious symptomatology	10	13	6	13
40–31 Major impairment	15	19	11	24
30–21 Unable to function	9	12	8	17
20–11 Needs some supervision	0	0	0	0
10–1 Needs constant supervision	0	0	0	0
Not classifiable	2	3	0	0

[1] $n = 78$.
[2] $n = 47$.

Results

Forty-four percent of the patients studied showed marked signs of psychopathology and disturbances in social adjustment on the GAS (table 1). In 31 percent, these disturbances were so pronounced (according to the GAS definition) that hospitalization would be expected (Spitzer, Endicott, and Fleiss 1976).

The strong correlation between the GAS and other important outcome measures (table 2) indicates that the GAS accurately reflects the global ratings of psychopathology or social adjustment at followup ($r = .84–.88$). Its correlation with more specific measures of psychopathology—for example, the "paranoid-hallucinatory syndrome"—is weaker, but generally exceeds $r = .60$. The correlation between the GAS outcome score and such followup period variables as duration of occupational disintegration, hospitalization, and paranoid-hallucinatory symptoms tends to be lower ($r = .43–.60$), suggesting that the global state at followup does not necessarily reflect charcteristics of the followup period.

Another finding of note is that global ratings of psychopathology and social adjustment at followup are rather closely correlated (table 2). But ratings of more specialized aspects of psychopathology and social adjustment showed only a weak correlation. Further analyses demonstrated that there are different patterns of relationship between specific aspects of psychopathology and specific aspects of social adjustment. For example, inactivity during leisure time is more closely correlated to a depressive-apathetic syndrome ($r = .41$) than to a paranoid-hallucinatory syndrome ($r = .23$) at followup. The respective durations of paranoid-hallucinatory symptoms, occupational disintegration, and psychiatric hospitalization during the followup period are weakly correlated ($r = .25–.46$).

Among approximately 40 potential predictor variables tested in a product-moment correlation analysis, a number of variables proved to be statistically significant ($p < .05$) predictors of global outcome, measured by the GAS (table 3). The best predictors ($r \geq .35$) were duration of occupational disintegration during the 5 years preceding index admission, impairment of working ability in the year before index admission, personality change before index admission, poor psychopathological state on discharge, and self-rating factor of paranoid tendencies at discharge. High scores on these variables were correlated with a poor global outcome.

Analysis of correlations between

Table 2. Product-moment correlations of outcome criteria (n = 74–78)

	Paranoid-hallucinatory syndrome	Global psychopathological state	Personality change	Impairment of work ability	Impairment of social adjustment	Impairment of level of functioning (GAS)	Duration of occupation disintegration	Duration of psychiatric hospitalization	Duration of paranoid-hallucinatory symptoms
Paranoid-hallucinatory syndrome	1.00								
Global psychopathological state	0.72[1]	1.00							
Personality change	0.37[1]	0.68[1]	1.00						
Impairment of social ability	0.27[1]	0.54[1]	0.79[1]	1.00					
Impairment of social adjustment	0.50[1]	0.79[1]	0.69[1]	0.63[1]	1.00				
Impairment of level of functioning (GAS)	0.59[1]	0.88[1]	0.73[1]	0.64[1]	0.84[1]	1.00			
Duration of occupational disintegration	0.26[1]	0.39[1]	0.55[1]	0.62[1]	0.42[1]	−0.43[1]	1.00		
Duration of psychiatric hospitalization	0.41[1]	0.53[1]	0.51[1]	0.52[1]	0.46[1]	−0.53[1]	0.46[1]	1.00	
Duration of paranoid-hallucinatory symptoms	0.56[1]	0.59[1]	0.36[1]	0.28[1]	0.51[1]	−0.59	0.25[1]	0.24	1.00

[1] = $p < .05$.

Table 3. Predictors of global outcome[1]

	Predictors of global outcome (GAS)	Correlation coefficient
(−)	Higher socioeconomic status of the parents	.25
(−)	Premorbid working dysfunction	.27
(+)	More advanced age at first manifestation	.28
(+)	More advanced age at first hospitalization	.23
(+)	Precipitating factors before first manifestation	.28
(−)	Duration of psychiatric hospitalization (5 years before index admission)	.27
(−)	Duration of occupational disintegration (5 years before index admission)	.38
(+)	Lasting heterosexual relationship	.28
(−)	Impairment of working ability (1 year before index admission)	.39
(−)	Personality change (1 year before index admission)	.42
(−)	Diagnosis of schizophrenia	.25
(−)	Poor psychopathological state at discharge	.35
(−)	IMPS super-factor of organic syndrome at discharge	.30
(−)	IMPS super-factor of depressive-apathetic syndrome at discharge	.24
(+)	Ratio of amelioration of the IMPS super-factor of psychotic excitement	.28
(−)	Self-rating factor of paranoid tendencies at discharge	.39
(+)	Ratio of amelioration of the self-rating factor of paranoid tendencies	.40

[1] n = 74-78; for self-rating factors, n = 45-50. (+) = good prognosis; (−) = poor prognosis.

the predictor variables and other outcome criteria revealed that the prognostic significance of one variable for the GAS did not necessarily apply to other outcome criteria. Likewise, a variable that is a good predictor for one outcome criterion may not be predictive of outcome score on the GAS. The inclusion of variables that are predictive for other outcome criteria, but not for the GAS, expands the number of predictors.

Global or more specialized psychopathological predictors tended to correlate more closely with psychopathological variables at followup than with variables concerning social adjustment or duration of hospitalization. An analysis of three predictors and the corresponding outcome variables (table 4)—duration of occupational disintegration, duration of psychiatric hospitalization, and global rating of psychopathological state—revealed that each predictor variable correlates most closely with the corresponding outcome variable. There was only one exception: The duration of occupational disintegration correlates equally closely with the duration of psychiatric hospitalization during the followup period. As for psychopathological predictors, although the five IMPS syndromes on admission do not predict global outcome, the "depressive-apathetic syndrome" and the "organic syndrome"[2] measured at discharge are significantly correlated with global outcome (table 5). The prognostic value of psychopathology at discharge is enhanced when differentiated outcome ratings of psychopathology are considered—for example, the five IMPS syndromes (table 5). There are syndrome-specific links between the five IMPS syndromes at discharge and the five IMPS syndromes at followup; that is, the closest correlations exist between each syndrome at discharge and the same syndrome at followup.

To find a combination of predictors with the highest predictive value for global outcome (GAS), stepwise multiple regression analyses were performed on four sets of data: sociodemographic data, biographical and premorbid adjustment data, psychiatric history data, and index hospitalization data. The stepwise multiple regression analyses were performed for each data set alone and then for the five best predictors of each data set together (a procedure similar to that used in World Health Organization 1979). The best predictors of global outcome are (in hierarchical order) impairment of working ability during the year before index admission, age at first hospitalization, psychopathological state at discharge, duration of

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[2] This super-factor consists of the original factors of "retardation and apathy" and "disorientation."

Table 4. Product-moment correlations between predictor variables and outcome variables concerning psychopathology and social adjustment[1]

	Global psychopathological state at followup	Duration of psychiatric hospitalization during followup period	Duration of occupational disintegration during followup period
Global psychopathological state at discharge	.37[2]	.15	.11
Duration of psychiatric hospitalization before index admission	.23	.35[2]	.21
Duration of occupational disintegration before index admission	.32[2]	.52[2]	.47[2]

[1] $n = 74–78$.
[2] $p < .05$.

occupational disintegration during the 5 years before index admission, and precipitating factors before the first manifestation of psychosis. Together, these five variables explain 36 percent of outcome variance (table 6).

In this analysis psychopathological data were supplanted as predictors by data on social adjustment. To analyze the predictive value of psychopathological data alone, a stepwise multiple regression analysis of the psychopathological data on index hospitalization was performed. The five best predictors are psychopathological state at discharge, the IMPS super-factor "organic syndrome" at discharge, the IMPS super-factor "paranoid-hallucinatory syndrome" at admission, the clinical diagnosis of "schizophrenia," and the IMPS super-factor "depressive-apathetic syndrome" at discharge. These five variables explain only 20 percent of the outcome variance.

To examine whether the prognostic value of psychopathological data could be optimized by taking into account the self-rating data on paranoid tendencies and depression, the same analysis was per-

Table 5. Product-moment correlations between the 5 IMPS super-factors from discharge and followup[1]

	IMPS super-factors at followup				
IMPS super-factors at discharge	Psychotic excitement	Paranoid-hallucinatory syndrome	Depressive-apathetic syndrome	Phobic-compulsive syndrome	Organic syndrome
Psychotic excitement	.30[2]	.11	.11	.12	.04
Paranoid-hallucinatory syndrome	.21	.36[2]	.10	.12	.06
Depressive-apathetic syndrome	.02	.06	.32[2]	.24[2]	.28[2]
Phobic-compulsive syndrome	.14	.08	.12	.19	.04
Organic syndrome	.14	.16	.39	.24[2]	.37[2]

[1] $n = 74–78$.
[2] $p < .05$.

Table 6. Combination of the 5 best predictors of "level of functioning" (GAS)

5 best predictors	Impairment of work ability (1 year before index admission)	(−)
	More advanced age at first hospitalization	(+)
	Poor psychopathological state at discharge	(−)
	Duration of occupational disintegration (5 years before index admission)	(−)
	Precipitating factors before first manifestation	(+)
Variance explained by 5 best:	36%	
Variance explained by all:	62%	

(+) = good prognosis, (−) = poor prognosis.

Table 7. Best prediction of "level of functioning" (GAS) by psychopathological data

Without self-rating			With self-rating		
Psychotic excitement	D	(−)	*Paranoid factor*	*D*	*(−)*
Depressive-apathetic syndrome	D	(−)	Organic (= apathetic) syndrome	D	(−)
Psychotic excitement	A	(+)	*Depression factor*	*D*	*(−)*
Depressive-apathetic syndrome	A	(−)	Psychotic excitement	D	(−)
Paranoid-hallucinatory syndrome	D	(−)	*Depression factor*	*A*	*(−)*
Explained variance (in percent)					
31%			42%		

n = 45; (+) = good prognosis; (−) = poor prognosis; A = admission; D = discharge; self-rating scale items are in italics.

formed on the 45 patients for whom admission and discharge self-rating data existed. Initially, the analysis was performed without the self-rating factors, and subsequently these factors were included. The analysis without self-rating factors yielded a different combination of best predictors for the reduced sample (table 7) than for the original sample. After inclusion of the self-rating factors in the analysis, these factors displaced some variables rated by psychiatrists. The data set including self-rating factors explains a greater part of the variance than the one without them.

Discussion

Our finding that 44 percent of patients with schizophrenic and paranoid psychoses had global outcome scores in the lower half of the 100-point GAS score range corresponds well with the findings of the Washington field center of the IPSS (Hawk, Carpenter, and Strauss 1975). In that 5-year followup study, 30 percent of the schizophrenic patients had scores lower than 50 percent of the maximal global outcome score. Thus, only a part of the schizophrenic population is characterized by poor outcome—a conclusion that is also supported by the findings of many other recent followup studies (e.g., Harris et al. 1956; Brown et al. 1966; Achté 1967; Bleuler 1972; Strauss and Carpenter 1972; Astrachan et al. 1974; Affleck, Burns, and Forrest 1976; Bland, Parker, and Orn 1978; Huber, Gross, and Schüttler 1979; Achté 1980).

Scores of the GAS correlate well with the other global outcome ratings of psychopathology and social adjustment at followup. However, the GAS does not so well reflect the more differentiated ratings of state at followup or of state during the followup period. The correlations between these outcome criteria are relatively weak. Because concentration on any one outcome criterion is associated with a considerable loss of information, it has been suggested that multiple outcome criteria should be used (Keniston, Boltax, and Almond

1971; Strauss and Carpenter 1972). Outcome should be characterized not as a single entity but as an interrelationship of several, partly independent outcome functions.

Predictors of outcome have been extensively discussed in the literature dealing with the prognosis of schizophrenia (e.g., Langfeldt 1956; Vaillant 1962; Phillips 1966; Stephens 1970; Bleuler 1972; Astrachan et al. 1974; Astrup 1975; Ciompi and Müller 1976; Pokorny et al. 1976; Goldberg et al. 1977; Huber, Gross, and Schüttler 1979; World Health Organization 1979). Among those variables that assumed the greatest prognostic significance in our own study, duration of occupational disintegration before index admission, as well as previous hospitalization, was a strong predictor in studies by Strauss and Carpenter (1974, 1977). The prognostic value of the psychopathological state at discharge was emphasized by Renton et al. (1965), Affleck, Burns, and Forrest (1976), and Wittenborn, McDonald, and Maurer (1977).

A personality change, especially in the sense of a loss of emotion, is another predictor that has been described by many authors (Vaillant 1964; Lindelius 1970; Stephens 1970; World Health Organization 1979). The present study is the first in which self-rating data on paranoid tendencies have emerged as prognostically important—perhaps reflecting the fact that self-rating scales have usually not been employed in followup studies of schizophrenic patients.

When outcome criteria other than GAS scores were considered, it was found that, in general, psychopathological variables were the best predictors of psychopathological outcome, and data on social adjustment (occupational disintegration, hospitalization) before index admission were the best predictors of social adjustment at followup. But there also were prognostic relationships among these different areas. Thus, the model of an "open-linked system" among different areas of predictor variables and outcome variables, postulated by Strauss and Carpenter (1974, 1977), was supported.

In an analysis of the correlations between the five IMPS syndromes at admission and followup, as well as at discharge and followup, the psychopathological state at discharge proved to have much greater prognostic value than that at admission. Moreover, the relationships between the five IMPS syndromes at discharge and followup were syndrome-specific. The prognostic importance of differentiated psychopathological data at discharge was also noted by other authors (Mintz, O'Brien, and Luborsky 1976; Goldberg et al. 1977; Wittenborn, McDonald, and Maurer 1977). In the IPSS such relationships could not be detected because psychopathological state was assessed on an index day but not at discharge (Strauss and Carpenter 1974, 1977; World Health Organization 1979). In accord with our findings, Strauss and Carpenter (1977) observed that the psychopathological data at 2-year followup were closely correlated with those at 5-year followup.

The best prediction of global outcome could be made using a combination of five predictors, identified by a stepwise multiple regression analysis. Together, these five predictors explained 36 percent of the outcome variance. Within this combination, impairment of working ability 1 year before index admission was the most important predictor. In contrast to the findings of the IPSS (World Health Organization 1979), psychopathological variables were included among the five best predictors. This discrepancy might be explained by the fact that in the IPSS psychopathological state at discharge—prognostically important in our study—was not recorded.

When only psychopathological variables were considered, the five best predictors could explain only about 20 percent of the outcome variance. The prognostic value of psychopathological variables could be optimized by inclusion of the self-rating factors concerning depression and paranoid tendencies.

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Depressive States Occurring During the Neuroleptic Treatment of Schizophrenia

by Hans-Jürgen Möller and Detlev von Zerssen

Abstract

Depressive states are often observed during the hospitalizations of acutely schizophrenic patients. But only a few studies have examined the frequency and course pattern of these depressions. In our investigation of 81 patients suffering from schizophrenic or paranoid psychoses and undergoing neuroleptic treatment, we found that the frequency and intensity of depression decreased from admission to discharge. On admission, 63 percent of patients showed a marked depressive apathetic syndrome, as compared to only 23 percent on discharge. Patients' self-rating data from the Actual Mood Scale (filled out every other day) showed that only a small proportion of the patients developed a depression during hospitalization without having also been depressed on admission. An analysis of psychiatrists' admission and discharge ratings produced similar results. Our findings suggest that neuroleptics are unlikely to be the major cause of depressions in patients suffering from acute schizophrenic or paranoid psychoses.

The growing literature on depression that occurs during the treatment of schizophrenics, especially treatment with neuroleptics, indicates that this is an important clinical phenomenon (Simonson 1964; Bowers and Astrachan 1967; Heinrich 1967, 1969; Helmchen and Hippius 1967, 1969; Hoedemaker 1970; Roth 1970; Rada and Donlon 1975; McGlashan and Carpenter 1976; McKinnon 1977; Planansky and Johnston 1978; Singh and Kay 1979). But little is known about depressive states that occur during pharmacotherapy, and the scientific positions are often contradictory (Bohacek 1967; Donlon and Blacker 1973; Floru, Heinrich, and Witte 1975; McGlashan and Carpenter 1976*b*, 1979; Woggon and Angst 1976; Goplerud and Depue 1978, 1979; Van Putten and May 1978; Gross and Huber 1980; Hirsch and Knights, in press). Most reports describing these depressive states were based on clinical impressions, and only a few studies used standardized rating instruments. Even the constructs used to describe them—pharmacogenic depression, postpsychotic depression, and akinetic depression—are not well defined, and their empirical basis seems weak.

To broaden our knowledge about depressive states that occur during neuroleptic therapy, we used data from our clinical documentation system (Barthelmes and von Zerssen 1978) for a group of schizophrenic inpatients to study the frequency and course pattern of depressive states.

Methods

Eighty-one patients admitted to the Max Planck Institute of Psychiatry (MPIP) in the period 1972–74 were studied. Based on ICD criteria (World Health Organization 1978), 67 patients (77 percent) were diagnosed by the ward psychiatrist as schizophrenics (ICD

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295)[1] and 19 (23 percent) as suffering from paranoid psychoses (ICD 297, 298.2, and 298.3).[2] Diagnoses were discussed in the weekly diagnostic conference under the supervision of the Head of the Department (von Zerssen) or his alternate (Mombour). Agreement between clinical diagnosis and a computer-derived diagnosis (DiaSiKa Program; von Zerssen, in preparation) was very high—88 percent for the diagnosis of schizophrenia, for example.

The group was almost equally divided between men (49 percent) and women (51 percent). Sixty-six patients (82 percent) were 40 years old or younger, and only one patient was over age 60.

Initial onset of illness had occurred before age 40 in 90 percent of the patients, was of an insidious nature in 27 percent, and was preceded by precipitating events in 44 percent. Admission to the MPIP was the first to a psychiatric hospital for 60 percent of the sample. Only 10 percent of the patients had been hospitalized previously for more than 200 days. During their stay in the MPIP, the patients were treated with neuroleptics (mostly haloperidol in individualized—but not high—dosages) and sociotherapy. Anticholinergics were administered generously if extrapyramidal side effects occurred. Antidepressant drugs were given only in the event of severe depressive or apathetic states. Hospital stay was 1 month or less in 18 percent of the patients, 3 months or less in 75 percent, and over 4 months in 8 percent. Usually 1 to 2 weeks before discharge, medication was changed from an oral to an intramuscular depot neuroleptic. At discharge, most patients either were in full remission or showed markedly reduced levels of symptomatology (Möller et al., 1981).

Standardized and well-validated rating instruments were used to describe the psychopathological state: the Inpatient Multidimensional Psychiatric Scale (IMPS; Lorr and Klett 1967; Lorr 1974) and the Clinical Self-Rating Scales (von Zerssen 1976). An advantage of the latter is the availability of normative values from a representative sample of the population of the Federal Republic of Germany. At admission (before the institution of neuroleptics) and discharge, the treating psychiatrist rated the patients using the IMPS. The patients themselves filled out the following scales from the Clinical Self-Rating Scales: the Beschwerdenliste (Complaint List; B–L), which measures vegetative and somatic complaints; the Paranoid-Depressivitäts-Skala (Paranoid-Depression Scale; PD–S), which measures relatively enduring depressive states; and the Befindlichkeits-Skala (Actual Mood Scale, Bf–S), which measures rapid fluctuations of mood. The Actual Mood Scale was administered not only at admission and discharge but also, in alternation with the parallel form (Bf–S'), every other day during the patient's hospital stay.

Mean scores and frequencies of defined syndrome levels at admission and discharge were calculated for the three IMPS factors indicating depressive, apathetic or neurasthenic symptoms—anxious depression, retardation and apathy, and impaired functioning—and their super-factor depressive apathetic syndrome (von Zerssen and Cording 1978). The same was done with the complaint and depression factors from the Paranoid-Depression Scale. In addition, configuration frequency analyses (Krauth and Lienert 1973) on defined syndrome levels (0, 1–20, 21–100 percent of the maximum scale) were carried out to evaluate the frequency of improvement or deterioration of depression between admission and discharge on a single case level.

The Actual Mood Scale data were analyzed in two ways. A computer program calculated the frequency of depressive periods as follows: The beginning of a depressive period was defined as a sequence of at least three mood scores higher than 21 (mean score of the normal population ± 1 standard deviation = 13 ± 8). The end of a depressive period was defined as a sequence of at least three scores below this value. The frequency of these depressive periods was related to the mean score of actual mood during the week of admission. In addition, the actual mood course was plotted for each patient. A typology of these curves was made by visual analysis, and an attempt was then made to classify the individual actual mood courses using this typology.

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[1] Patients with schizoaffective disorders (ICD 295.7) were excluded to avoid confusing their typical endogenous depression with the depressive states occurring in neuroleptic-treated schizophrenics.

[2] Only four patients were included in the last two groups (i.e., ICD 298.2 and 298.3).

Results

A detailed report of findings concerning depression on admission and discharge, measured by the IMPS and the PD–S and B–L, has been published elsewhere (Möller and von Zerssen 1981). Therefore, these results will only be briefly summarized here. Depressive states occur frequently during acute schizophrenic and paranoid psychoses. For example, 50 percent of patients had a marked intensity (more than 20 percent of the maximum scale) of "anxious depression" on admission, and 63 percent had a marked intensity of the "depressive-apathetic sydrome" (table 1). The mean scores of depressive syndromes (Wilcoxon test, $p < .01$) and the frequency of depressive syndromes of marked intensity decreased between admission and discharge (Bowker test, $p < .01$). However, at discharge, there was still a marked intensity of "anxious depression" or "depressive-apathetic syndrome" in 21 and 23 percent of patients, respectively. Most patients who suffered from a depressive syndrome at discharge had already had a depressive syndrome of the same or greater intensity on admission (table 2). Only about 10 percent of the patients were more depressed at discharge than on admission. Findings for self-report data were similar.

Table 1. Frequency of defined intensities of depressive syndromes on admission and discharge

		Relative frequency (percent)	
IMPS (*n* = 81)	**Syndrome level**	**Admission**	**Discharge**
Anxious depression	0	3	1
	1–20	47	78
	21–50	42	21
	51–100	8	0
Retardation and apathy	0	11	29
	1–20	36	48
	21–50	44	21
	51–100	9	2
Impaired functioning	0	15	43
	1–20	10	13
	21–50	26	33
	51–100	49	11
Depressive-apathetic syndrome	0	1	0
	1–20	35	78
	21–50	62	22
	51–100	1	1
Clinical Self-Rating Scales (*n* = 50–68)			
Depression	0[1]	2	6
	1–20[1]	31	48
	21–50	36	36
	51–100	32	10
Somatic complaints	0[1]	9	11
	1–30[1]	42	67
	31–50	31	18
	51–100	18	6

[1] Normal

Analysis of the actual mood fluctuations during hospitalization provides additional insight into the course of depressive disturbances. After the elimination of patients with a very short hospital stay (below 20 days) or for whom incomplete data were available, there remained a group of 72 patients whose actual mood courses could be analyzed. Only 29 (40 percent) of them showed no defined depressive period; the remaining 43 (60 percent) suffered one (33 percent) or two or more (27 percent) depressive periods, respectively. Only 11 (15 percent) of the 72 patients developed a depressive period during hospitalization without also having been depressed on admission. Depressive periods were overrepresented (table 3) in patients with an actual mood score higher than 21 on admission (χ^2 test, $p < .01$): 82 percent of these patients suffered depressive periods during hospitalization compared to only 33 percent of patients with normal actual mood scores on admission. A simple calculation produced

Table 2. Frequency of defined patterns concerning change of depressive syndromes (in percent)

	IMPS (*n* = 81)				Clinical Self-Rating Scales (*n* = 40)
Type of change	Anxious depression	Retardation and apathy	Impaired functioning	Depressive-apathetic syndrome	Depression
No change	56	50	48	51	65
Amelioration	35	42	41	44	30
Deterioration	9	8	11	5	4

No change = same score level at admission and discharge; amelioration = reduced score level at discharge; deterioration = increased score level at discharge.

Table 3. Frequency of "depressive periods" (measured by the Actual Mood Scale)

Actual mood on admission	Frequency of "depressive periods"			
	0	1	2	>2
Mean ≤ 21 ($n = 33$)	22 (67%)	7 (21%)	2 (6%)	2 (6%)
Mean > 21 ($n = 39$)	7 (18%)	17 (44%)	8 (21%)	7 (18%)
$n = 72$	29	24	10	9

similar results: the 39 patients with a depressive mood score on admission suffered 1,111 depressive days, as measured by the actual mood score, compared to 143 days for the 33 patients with a normal mood score on admission (χ^2 test, $p < .01$).

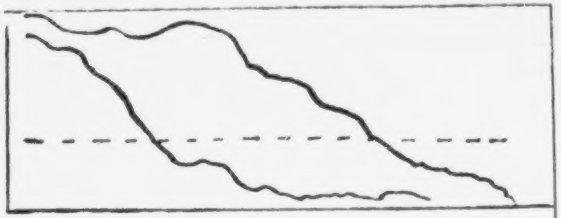
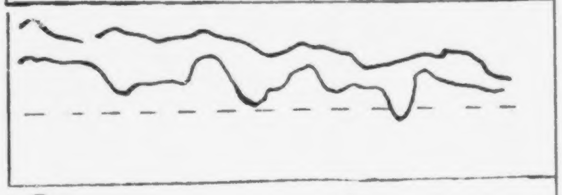
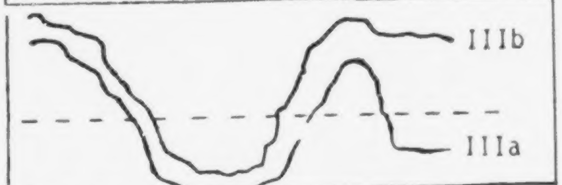
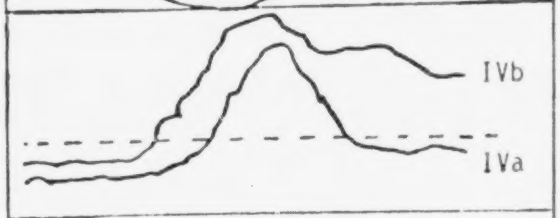
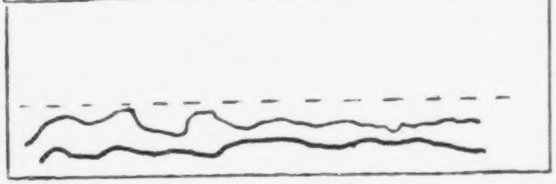
Figure 1 illustrates the types of courses characteristic of the patients' hospital stays: no depression ($n = 19$, 26 percent); constant depression ($n = 17$, 24 percent); decreasing depression ($n = 16$, 22 percent); newly developed depression without depressive mood on admission ($n = 12$, 17 percent); recidive depression after depression on admission ($n = 6$, 8 percent). The distribution of frequency of newly developed depressions was unimodal and reached a maximum during the 5th or 6th week of hospitalization.

Discussion

Our findings that many patients with acute schizophrenic or paranoid psychoses suffer not only from schizophrenic symptoms but also from marked depressive, apathetic, and neurasthenic symptoms is in agreement with other reports in the literature (Lorr and Klett 1967; Mombour 1974; McGlashan and Carpenter 1976*a*; von Zerssen 1980). In our study, 63 percent of the patients had a marked "depressive apathetic syndrome" on admission. At discharge, 23 percent of the patients—most of whom were in remission from psychosis but undergoing neuroleptic treatment—showed signs of a marked "depressive apathetic syndrome." This rather high frequency of depression on discharge coincides with the clinical observations concerning "pharmacogenic" or "postpsychotic" depressions (Bowers and Astrachan 1967; Heinrich 1967; Steinberg, Green, and Durell 1967; Helmchen and Hippius 1969; Roth 1970; Shanfield et al. 1970; Stern, Pillsbury, and Sonnenberg 1972; McGlashan and Carpenter 1976*a*, 1976*b*). However, the hypothesis of a "pharmacogenic" (drug-induced) or "postpsychotic" (psychogenic) depression is not supported. In fact, the intensity and frequency of depressive symptoms decreased from admission to discharge—a pattern also observed by Shanfield et al. (1970), Woggon and Angst (1976), von Zerssen (1980), and Hirsch and Knights (in press). Only from 5 to 10 percent of patients (the percentage depending on the syndrome in question) were more depressed at discharge than on admission—a finding which does not provide strong support for the concept of "pharmacogenic" or "postpsychotic" depression.

Psychiatrists' ratings showed good agreement with the patients' self-ratings, which is important because the self-ratings were not completed by all patients. Self-rating scales have rarely been used

Table 4. Course patterns of actual mood ($n = 72$)

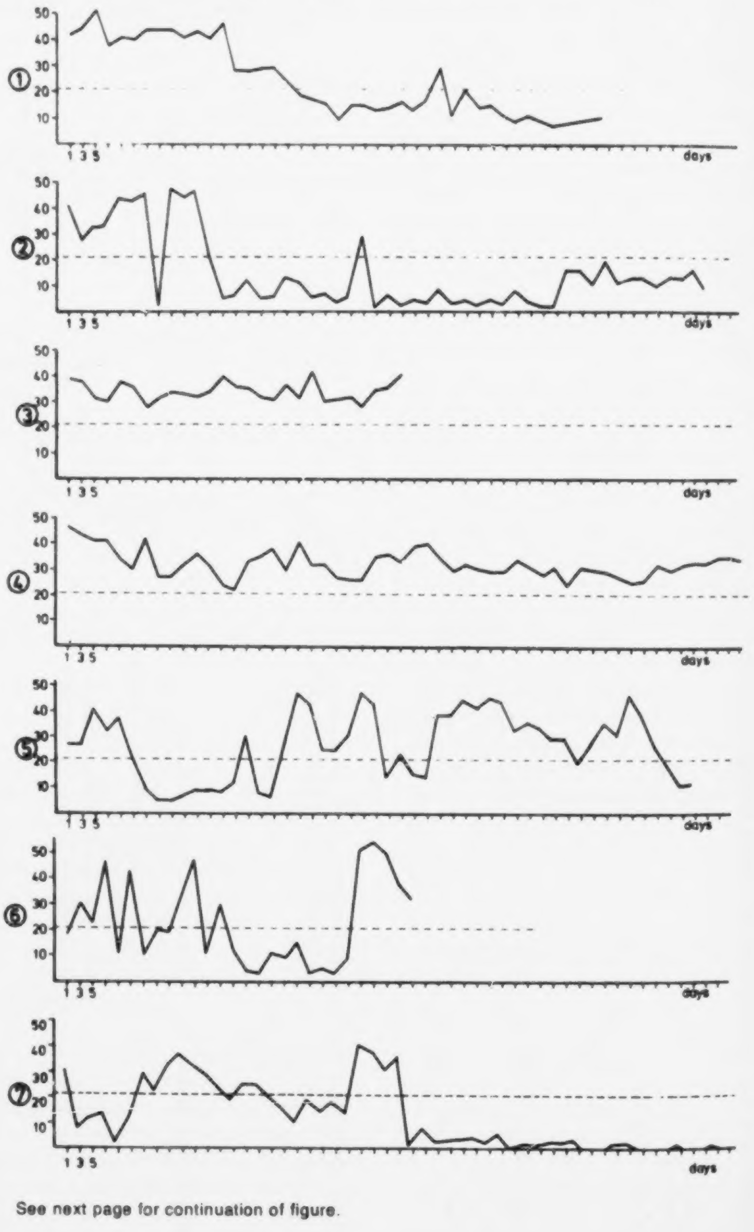
Course pattern of depression	Description	Graph	Frequency
I. Decreasing depression	Depressive mood scores on admission, decreasing scores during hospital stay		16 (22%)
II. Constant depression	Depressive mood scores during (approximately) the whole hospital stay		17 (24%)
III. Recidive depression	Depressive mood scores on admission, after decreasing to normal scores, development of one or more depression periods a. normal scores on discharge b. depressive scores on discharge		6 (8%) IIIa.4 IIIb.2
IV. Newly developed depression	Normal mood scores on admission, development of one or more depressive periods during hospital stay a. normal scores on discharge b. depressive scores on discharge		12 (17%) IVa.7 IVb.5
V. No depression	No depressive mood scores during (approximately) the whole hospital stay		19 (26%)
VI. Others	Not classifiable		2 (3%)

in studies of depressive or similar states in schizophrenics, but two studies which did use self-ratings also found a decreasing intensity of depression or physical complaints during the period between admission and discharge (Shanfield et al. 1970; von Zerssen 1981).

The Actual Mood Scale results are of particular interest because the frequent measurements (every other day) provide a detailed picture of the course of depressive states. Fifty-six percent of the 72 inpatients for whom Actual Mood Scale data were available showed depressive mood for at least 1 week during hospitalization; but only 15 percent of the 72 patients showed such mood without having been depressed on admission. Our analysis of graphical representations of actual mood data from each patient identified a number of typical course patterns. The most frequent patterns were (in descending order of frequency): no depression, constant depression, decreasing depression, and newly developed depression without depressive mood on admission. The last type characterized 17 percent of the patients, which accords well with the calculations given above.

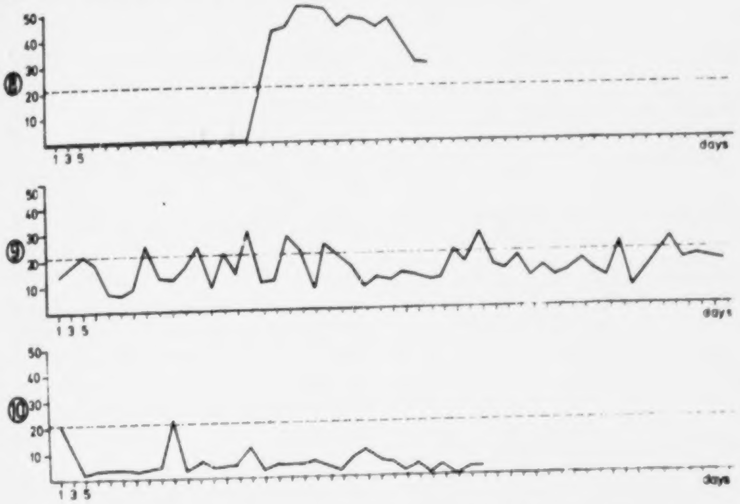
A methodological problem in the present study, and indeed in all previous ones, is the fact that dosages of neuroleptics were not standardized; anticholinergics were administered to most patients; and antidepressants were administered to 14 percent. Treatment with anticholinergics or antidepressants, of course, might have reduced depressive symptoms (Rifkin, Quitkin, and Klein 1975; Van Putten and May 1978; Prusoff et al. 1979). A second

Fig. 1. Original "actual mood" curves, selected to demonstrate typical patterns of course (see table 4)



See next page for continuation of figure.

Fig. 1. Original "actual mood" curves, selected to demonstrate typical patterns of course (see table 4)—*Continued*



problem is that medication used before admission was not well documented. Based on our experience, we assume that most of the patients had not been on continuous medication before admission and that many were free of neuroleptic medication when admitted. Medication history is an important factor because lengthy exposure to neuroleptics has been hypothesized to cause depression (Helmchen and Hippius 1967; Floru 1975). Therefore, we are now gathering more complete data concerning prior medication from the records. Despite these methodological problems, our study has the advantage, compared to earlier ones, of a large patient sample, standardized ratings obtained from both psychiatrists and patients, and the exclusion of patients with schizoaffective psychoses.

We believe our findings suggest that so-called "postpsychotic depression" mostly results from an overhang of depressive symptoms that accompany florid psychotic signs. When the psychosis resolves, the depression is unmasked. Only a small proportion of patients (5 to 17 percent, depending on the syndrome in question and the method of analysis) were depressed during hospitalization without also having been depressed on admission. It is possible that these depressions were caused by neuroleptics ("pharmacogenic depression") or psychoreactively induced by the remission of psychosis ("postpsychotic depression" in the strict sense). Our medication history data are too incomplete to permit us to differentiate between the possible causes of depression on admission. If the depressive states had been caused by neuroleptics, one might have expected levels of depression to increase during the first weeks of hospitalization as dosages of neuroleptics were increased; but this pattern characterized only a very small proportion of the patients studied. Because of the methodological problems mentioned above, however, firm conclusions about the depressiogenic effect of neuroleptics cannot be drawn.

Postscript

After this article was completed, we received a manuscript from Strian, F.; Heger, R.; and Klicpeva, C.: The time-structure of depressive mood in schizophrenia. *Acta Psychiatrica Scandinavica,* in press. These authors arrived at similar conclusions to our own using another method of analyzing Actual Mood Scale data.

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Aphanisis: The Syndrome of Pseudo-Depression in Chronic Schizophrenia

by Thomas H. McGlashan

Abstract

A syndrome of psychic blankness, or pseudo-depression, here labeled aphanisis, is seen commonly in chronic schizophrenic patients. It is frequently confused with and misidentified as a postpsychotic depression. Clinical observations deriving from a setting of intensive psychotherapy with three chronic schizophrenic patients are compared with recent information concerning the normal and pathological development of affects in children to identify the state of aphanisis as distinct from states of depression phenomenologically, developmentally, and psychodynamically. Careful scrutiny reveals aphanisis to be an actively maintained regressive or primitive psychological state of an autistic nature serving important defensive/adaptive aims. Discussion highlights the differential diagnosis between aphanisis, postpsychotic depression, and maturational grief and how this may help reduce heterogeneity in the sampling of various postpsychotic syndromes for treatment and research purposes.

"The most important part of a person's life is his affect."
—Elvin Semrad (Quoted in Rako and Mazer 1980, p. 27)

The purpose of this article is to describe and explore a state of psychic blankness, here labeled "aphanisis," which is common to the so-called "burned out" chronic schizophrenic patient. This state is often overlooked because of its silent nature compared with the more florid symptoms and behavioral aberrations that characterize the acute phases of schizophrenic breakdown and exacerbation. Nevertheless, the "quiet" obliteration of the patient's inner world that often accompanies the schizophrenic process, though less obvious, is no less important to describe and study. Careful clinical observation, in fact, may reveal it to be a distinctive syndrome: hence, the application of a new descriptive label—aphanisis. In the past, such a state has usually been classified as and confused with a postpsychotic depressive syndrome. Here, it will be distinguished from such depression phenomenologically, developmentally, and psychodynamically, and shown to be an actively maintained regressive or primitive psychic state of an autistic nature serving important defensive aims.

Heterogeneity of Postpsychotic Depression in Schizophrenia

In a review of the literature on postpsychotic depression in schizophrenia, McGlashan and Carpenter (1976*b*) gathered a variety of clinical pictures into the following composite description:

> The clinical picture most frequently resembles that of a retarded (and, less often, agitated)

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> depression with massive inertia and frequent neurasthenic complaints. Strong schizoid elements are usually present such as complaints of emptiness, or lack of feelings. There is paralysis in interpersonal relations; the patient fails to *actively* contact others, yet through enormous *passivity* he regressively demands care and attention from all around him. Suicidal ideas and acts are common, making this time no less dangerous (and perhaps more so) than the acute episode. This clinical picture is usually stable, and duration is variable from weeks to more than a year. During this time the patient is often resistant to all modalities of treatment. . . . [p. 238]

As an attempt to integrate scattered reports of this syndrome, this composite description imparts an appearance of homogeneity which, in fact, may not exist. Indeed, subsequent work has highlighted that postpsychotic depression (PPD) in schizophrenia probably represents a heterogeneous collection of syndromes. Returning to the basics of clinical description, we find that PPD is far from a unitary phenomenon. Kayton, Beck, and Koh (1976) preferred the term postpsychotic *regression* to describe this state rather than postpsychotic *depression* because they found depression per se such a variable feature. Planansky and Johnston (1978) identified the frequent occurrence of depressed mood, feelings of worthlessness, low self-esteem, and guilt with self-reproach in a review of the records of 115 VA schizophrenic patients. Although this may appear distinctly "depressive" in quality, the authors go on to state:

> The depressive syndrome in our schizophrenics resembles . . . an extreme form of negation . . . [in which] the patient denies his own existence, or the existence of the whole world. . . . "Leave me alone, I am dead" was the final self-separating statement of one of our patients who had an early history of a typical guilt syndrome, but had long since been stabilized in a quiet, unproductive attitude of schizophrenic non-involvement. [p. 215]

The latter sound far more like what is called residual schizophrenic defect than a turbulent or painful depressive syndrome, thus making it hard to know what the authors mean by "depression." Donlon, Rada, and Arora (1976) suggest that depression in resolving schizophrenia may often be confused with residual symptoms of schizophrenia and drug-induced akinesia. Van Putten and May (1978) describe two types of clinical pictures (both of which they maintain are drug induced). The first they label postpsychotic depression, consisting of subjective feelings of sadness, hopelessness, gloom, suicidal ideation, and despondent mood. The second they label "pseudo-depression," consisting of silence, apathy, emotional unresponsiveness, and indifference to surroundings. Such heterogeneity of clinical description has recently led several clinician-investigators (Hartmann et al. 1980) to note the need for careful differential diagnosis between (at least) three postpsychotic states: (1) drug-induced or akinesia-related depressive syndromes, (2) reactive postpsychotic depression, and (3) residual schizophrenic defect.

Independent of clinical description, evidence for the heterogeneity of postpsychotic states has accumulated from studies of etiology, outcome, and medication responsiveness. Etiologically, Van Putten and May (1978) maintain that most episodes of PPD are secondary to neuroleptic-induced akinesia (Rifkin, Quitkin, and Klein 1975), which can be reversed, like many other neuroleptic side effects, with antiparkinsonian medications. On the other hand, although McGlashan and Carpenter (1976*a*) originally noted a correlation between PPD and neuroleptics, many patients in their sample who became depressed were also drug free. Thus some forms of PPD appear more drug related, whereas others do not.

Looking at outcome, Mandel et al. (in press) demonstrated a significantly elevated risk of relapse and rehospitalization if schizophrenic patients developed PPD. Kayton, Beck, and Koh (1976) and McGlashan and Carpenter (1976*a*), however, found no such relationship between relapse and the appearance of PPD over 1- to 3-year followup periods. Such disparate findings may represent an artifact of heterogeneity; that is, the patients labeled as depressed in one study may not be the same psychopathologically as those assigned the same label in a different study.

Heterogeneity may also account for the equivocal results obtained with drug treatment. Studies of the use of lithium (Van Kammen, Alexander, and Bunney 1980) and antidepressants alone (Siris, Van Kammen, and Docherty 1978) or in combination with neuroleptics (Siris, Van Kammen, and Docherty 1978; Prusoff et al. 1979) for the treatment of the schizophrenic patient who becomes depressed highlight the variability of response. Some patients get better, others become worse, and many evidence no change. Siris, Van Kammen, and Docherty (1978) noted that a subgroup of schizophrenic patients with "symptoms of clinical depression other than anergia" appeared to benefit most consistently from the addition of an antidepressant. These findings suggest the existence of separate syndromes within the domain of PPD, some of which are responsive to pharmacologic intervention and some of which are not.

Depression Versus "Burn Out"

Most descriptions of postpsychotic depressive phenomenology appear to cluster in one of two directions. Many of the reported signs and symptoms (McGlashan and Carpenter 1976*b*) describe a syndrome more characteristic of primary affective disorder. These are: psychomotor agitation or retardation, insomnia, loss of libido, hypochondriacal concerns, suicidal preoccupations, and feelings of sadness, guilt, hopelessness, and helplessness.[1] The other cluster of signs and symptoms (McGlashan and Carpenter 1976*b*) gives the impression of affective poverty or absence. These are: motivational inertia, interpersonal isolation, anhedonia, and reports of feeling empty, stuck, or *blank*. Such phenomena often lead to a schizophrenic patient being regarded as "burned out," "flat," "demoralized," or in a "residual defect" state.

It is the intention here to describe this state of blankness in schizophrenia from several perspectives—phenomenology, emotional development, and psychodynamics; to demonstrate that these blank states represent a form of psychic organization that is more primitive developmentally and structurally than depression; and, it is to be hoped, to aid in clarity of identification and differential diagnosis, thus enhancing homogeneity of sampling for treatment and research purposes.

Case Descriptions

Case No. 1: Dorothy. Dorothy was a 29-year-old, white, single female who had been ill for 10 years. Since her first break at 19, she had undergone six hospitalizations over the 6 years before her admission to Chestnut Lodge at age 25. During unmedicated periods over her first 4 years at Chestnut Lodge, she manifested severe fragmentation with multiple delusions, auditory, visual and tactile hallucinations, and marked thought disorder. Predictably, within 2 months of the institution of neuroleptics (20 to 40 mg of trifluoperazine), she would organize to a non-*floridly* psychotic state. She demonstrated an absence of major distortions of reality in her social discourse, and she was no longer a daily nursing "management problem." She recognized her status as a patient and acknowledged me as her therapist. If she continued to experience delusional thoughts or hallucinatory perceptions, she kept them private. When medicated, Dorothy demonstrated characteristic pseudo-depressive symptoms: low energy, blankness, passivity, withdrawal, and complaints that any activity was "too much." She was also prescribed antiparkinsonian drugs (benztropine mesylate, 4 mg/day), making it unlikely that her clinical picture resulted from drug-related akinesis. Furthermore, she seldom if ever appeared drowsy, a clinical sign of akinesis described by Van Putten and May (1978) and Van Putten, May, and Wilkins (1980).

In her partially remitted state, Dorothy frequently complained of anxiety and depression. Nevertheless, upon closer inspection these affects never appeared very differentiated either from one another or as identifiable affects per se. She described this anxiety and depression as tiredness, exhaustion, or a diffuse, vague, global fear of "life." At times, this affect was concretely somatized as physiological discomfort without psychic components. For example, she described anxiety as a "squishy" feeling in her head which she wanted to relieve via lobotomy or literally by "wringing out" her brain. The sensations were vague, unpleasant "stretching and pins and needles" feelings on the left side of her head and buccal mucosa. Two neurologic consultations failed to reveal any organic pathology to these Isakower-like sensations (Isakower 1938; Lewin 1955). Her discomfort could also be a "part-body" experience (e.g., one time she said her head was tense while her arms and legs were relaxed). Virtually always, Dorothy reported these feelings and sensations as overwhelmingly unpleasant or dysphoric. She once described herself as rendered helpless and handicapped like a quadriplegic by this anxiety.

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[1] The appearance of such signs and symptoms often calls into question the original diagnosis of schizophrenia. In some cases a change in diagnosis to affective disorder may indeed be warranted. Nevertheless, affective symptoms can also be part of an established schizophrenic illness (McGlashan and Carpenter 1979). It is to this group that we apply the term PPD.

Dorothy demonstrated a limited repertoire of coping strategies to defend against this unpleasant experience. One set of strategies seemed to involve attempts to *obliterate internal stimulation* (i.e., to "blank out" thoughts and affects). She reported, for example, often succeeding in having no thoughts, which imparted a feeling of being "secure." Her ultimate weapon against anxiety was a compulsive thought, "Think blank." She combatted "bad" thoughts like "I didn't get help in high school" with "good" thoughts like "I got help in high school." When the latter dominated, she felt whole, calm, and "perfect." When the former dominated, she experienced intense dysphoria, fears of being "horrible," irreversibly sick, and overwhelmed by her "cruel childhood." Sometimes Dorothy's defensive, compulsive thoughts appeared to contain a somatic equivalent. Often she became very still and her breathing would become quick, shallow, and measured at first, to be followed by one or more deep sighs. It was difficult to know what was transpiring since she usually remained silent. One day, however, she said, "I think unpleasant thoughts like 'WSH' [her high school] and think I'm the worst person in the world, and I try to think of the vivid colors of God's help, but I can't quite think of it. Or I will breathe three or four times and concentrate on the breathing and think about the thought of taking a deep breath after the short ones and I try to get just that thought, but usually I can't." In short, Dorothy seemed to link the process of thinking with the process of breathing, as if with certain breaths she might create a barrier to inner dysphoria.

Another set of coping strategies appeared to involve attempts to *obliterate external stimulation.* Her daily behavior minimized stimulation. If allowed, she preferred to stay in bed all day long (never asleep—just in bed). She preferred silence and once remarked, "Silence means nothing is, like your existence is just nothing." In our sessions she was usually silent and clearly experienced my attempts to communicate as intrusions on her blank equanimity. I often felt she was using me and my office as if we were seclusion room walls and that she regarded me at such times as no more animate than the chair in which she sat.

These efforts appeared to represent Dorothy's attempts to substitute some kind of stimulus barrier for a defective repressive and/or screening capacity. In her passivity and silence, Dorothy appeared to demonstrate the quintessence of "negative" or "defective" symptoms of the "burned out" schizophrenic. In contrast to her appearance, however, she was not "void" of psychological activity. She strove to maintain low stimulation from minute to minute and the effort extorted enormous amounts of her daily energy. Once, in a rare voluble moment, Dorothy indicated how hard it was to face each new day. She said, "In my apartment before I came here I used to stay in bed all the time. If I got up, I would go to the couch and lie down and watch TV. I did that here too until the unit locked me out of my room during the day. But it's too much! It takes it all out of me! I guess it's better they are doing it because then I'm not so lazy, but it's so hard!"

At times when silence and blankness seemed impossible to achieve, Dorothy attempted to *scotomatize* (Segal 1957) *external and internal stimulation* by, paradoxically, fixing or focusing her attention on specific thoughts and ideas or external noises instead of trying to obliterate everything. At the beginning of one session she said, "I feel I exist but I don't know who I am. . . . I can't stand the thought of sleepless nights without my radio on." Later in the same session she reported feeling less discomfort now that she had come to my office and noted, "I told myself I was Dorothy who was not sure who I am, but I'm still Dorothy coming to your office." I felt she was using this thought in the session much as she used her radio at night: to provide some focus on which to narrow her attention and screen out everything else.

Case No. 2: Sam. When Sam entered Chestnut Lodge, he was 26 years old, single, and had been continuously ill since age 17. Before his transfer he had experienced 12 previous hospitalizations and the entire array of current therapeutic interventions. When unmedicated, he was deeply engrossed in a confused psychotic state replete with paralyzing ambivalence and a severely fragmented delusional paranoid experience in which he literally felt assaulted by painful tactile hallucinations. During these times he paced in an agitated fashion back and forth across his room (where we held our sessions), muttering actively in response to hallucinated voices, and gesticulating stereotypically in a manner that led me to believe he was ritualistically trying to "shoo away" impinging thoughts or hallucinated persecutions. On occasion he would suddenly jump with a start, grab his leg or head, and look at me with hate as if I had just punched him from across the room.

When medicated (trifluoperazine, 10 to 30 mg/day plus benztropine mesylate, 4 mg/day), he was usually silent and would lie immobile on his bed (again while awake). As was true of their dealings with Dorothy, staff encountered enormous daily difficulty mobilizing him out of his room. He appeared passive, withdrawn, completely lacking in initiative, and silently out of touch with other patients and staff. Unlike Dorothy, however, Sam's state of pseudo-depression seemed less stable or less resistant to regressive fragmentation. At times, if pushed too much by others to relate, he would suddenly break out of his immobility and begin pacing agitatedly, muttering and gesticulating as before. At times, an overload of thoughts or feelings arising internally seemed sufficient to trigger a period of agitation, even without external intrusion. When he was medicated, such agitated periods were never as agonizing or unrelenting as when he was drug free. They would eventually subside after several hours, and Sam would pass over once again into a state of immobility.

During periods of pseudo-depression, Sam appeared, like Dorothy, to be scotomatizing stimulation. When verbal at these times, he reported that he was "meditating" or, as he said, "focusing my mind upon my body." With this "exercise," he eliminated all thoughts and feelings and strove to attain a tension-free focus on his body as an organic entity. If successful, he experienced an intact sense of himself as a body. This state also seemed to be idealized (e.g., he reported feeling "high" at such times). Lack of success at meditation, however, left him vulnerable to feeling "anger" and to experiencing sudden transformation into a "werewolf" or into an "anti-Christ" who could "destroy the world." I surmised that the latter experiences accompanied or triggered his abrupt resumption of agitated pacing.

Since Sam's intense dysphoria appeared particularly primitive and preverbal, I was usually left to guess its nature. During these agitated periods Sam seemed to be experiencing an elemental dread about possessing some powerful, aggressive, evil force inside himself capable of destroying his most cherished objects and himself. Once while pacing, he said to me, "Get out of here! I'm insane! You're breathing my air!" Later he told me that mental illness could be passed through the air like germs. While agitated, he often hid his face from me. Later I learned from him it was so I wouldn't see the flesh peeling off his evil skull, the sight of which he was convinced would destroy me by driving me insane.

During periods of pseudo-depression, Sam appeared to use omnipotent denial in his struggle to obliterate these particularly dysphoric affective states. One day, for example, he let me know about his "force field." In short, he told me that through meditation he created a "force field" around himself—an invisible shield protecting him against attack from the outside world and from persecution communicated along a "telepathic" network wherein various Himalayan gurus accused him of being evil. He added that should he feel or express anger, his shield could shatter and he would suddenly become "vulnerable."

After several years of psychotherapeutic work, Sam became more adept at putting the nature of his meditative experience into words. Once again, what he described sounded like a way of scotomatizing stimulation. One day, for example, he gave me the following lecture. "Do you remember the seven minds of meditation I taught you about 2 years ago? I've been thinking about a way to cure schizophrenia with them. I know you have your way of curing schizophrenia too, but I think mine is faster and more efficient. The way to heal schizophrenia is to get the seven minds into one mind. One way to do it is jogging. Jogging is one of the minds—the moving mind. If you jog and get a second wind, you are in the moving center of the brain and the other minds snap." I said I took this to mean that his experience was then somehow rendered homogeneous and he agreed. He added that another of the seven minds has an "instinctive center" that is connected with feeling pain. He said, "Feeling pain can cure you too. Some yogas feel pain all the time." He went on to elaborate some of the other "centers" of the mind—in each instance indicating that if you can become deeply engrossed enough in one form of sensory experience, other intruding experiences will be successfully obliterated, thus creating a kind of dictatorial but organizing hegemony of monochromatic sensation. Such total engrossment in one experience to the exclusion of everything else is how Sam constructed his meditative "force field" to shield against the uncontrolled intrusion of other stimuli which he experienced as persecutory.

Case No 3: Bill. Bill was a young man of 21 when he arrived at Chestnut Lodge. However, because his illness had begun in early adolescence at age 14, he had already experienced three previous hospitalizations covering a total of 2½ years. When unmedicated, he experienced multiple delusions and hallucinations of a paranoid and grandiose nature. He continued to experience these when medicated (trifluoperazine, 20 to 50 mg/day plus benztropine mesylate, 4 mg/day), albeit with diminished intensity and frequency. Unlike Dorothy and Sam, he was quite verbal and possessed a striking capacity to fluctuate in level of regression from moment to moment. As such, he proved remarkably capable of describing his subjective experiences.

Like Dorothy, Bill frequently experienced affects in a somatic mode. For example, he usually "felt" unpleasure as pains in his chest. He would begin rubbing his sternum and describe an ill-defined pain about his heart. In one session he recalled a past sojourn through a halfway house where he experienced "loneliness." When I asked what that felt like, he rubbed his chest saying it felt as if his heart were in pain. He described how he would lie in different positions on his bed trying to shift his heart into a less uncomfortable angle. I asked him whom he missed at the time and he clearly indicated—nobody. His body wanted succor and relief from pain; it involved no psychic elaboration of a nurturing object from whom he as a supplicant subject wanted something.

Bill seldom experienced differentiated feelings and regularly reported bafflement with people who did. Once he named five feelings: love, hate, greed, envy, and despair. Later in the session he forgot one of the names (envy). He became very distressed and experienced the loss of the word as the loss of the feeling itself. When he did report anxiety, it sounded rather primitive. For example, he told me about experiencing the "tension" on his inpatient unit as a concern that his spinal cord would be torn asunder rendering him quadriplegic. Another time he complained of tension in his body and said, "I have no one to pass the tension to. I used to be able to pass it to my father and other members of the family. My father was the easiest, although he was good at passing it too—by shouting." Then Bill began chanting, "Pass the meat, pass the potatoes, pass the peas, pass the tension." I inquired if his parents ever passed the tension back to him. "Oh yeah," he replied, "by putting me in places like this." When less regressed, he reported feeling depression (as it is usually understood), but added, "I get these pains in my legs and chest when I can't get depressed."

Bill seemed particularly facile at obliterating inner experience, usually by lying perfectly still, wide-eyed, and unblinking for long segments of therapeutic hours. Once he imparted a cogent description of the obliteration process itself. He showed me a science fiction novel given to him by his favorite student nurse. He displaced his idealization of her onto the book which he kept safely tucked away in his dresser, untouched and unread. He indicated that reading the book placed it in danger of being less than perfect (i.e., he might have *feelings* that it was poorly written or boring). Awareness of such negative feelings would shatter the book's perfection. I asked if that meant the perfect book would be turned to trash. "No," he replied, "then it is no longer a book!" In essence, unless he could totally protect the object from dysphoric feelings, it simply ceased to exist as a mental representation. In like fashion, he once reported that when I left our sessions he retained no idea of me whatsoever. Another time he said, "I have an assumption that I'm alive" and noted that he couldn't "hold onto" feelings about people from the past like his mother and father. In still another session, he said he was being kind to me to make up for "all the hurt I don't feel" (i.e., he had not come to "feel" as a result of therapy which he knew I wanted). He added, "You see, I would die if I was feeling. . . . I don't have natural reality like others because I'm not living. I'm always in a place of ever death. . . . You have a language that I don't understand though I know you want me to learn it. You want me to want."

Like Dorothy and Sam, Bill also used his bodily sensations and thoughts as objects upon which to scotomatize his attention. Once when talking (quite literally) about castrating women, he began running his hands through his hair and pulled up his shirt to expose and rub his stomach as if to reassure himself of his body's existence and intactness. He would often write down (secret) thoughts, then carefully fold the paper, seal it in an envelope, place it in his pocket, and then sit or lie silently like a statue. By this ritual he seemed to be defining himself and to be protecting this image from internal or external invasion.

Theoretical Considerations

To understand the state illustrated above, it is necessary to go beyond clinical description into the phenomenology of affect in human development and childhood psychopathology. Although the relevant literature (largely psychoanalytic) is voluminous, only points salient to our topic will be highlighted.

Affect in Normal Human Development. In Mahler's schema of human development (1961, 1966, 1968, 1971, 1972; Mahler, Pine, and Bergman 1975), the child's first major life phases are autism (0–2 months), symbiosis (2–8 months), and separation/individuation (8 months to 3 years). Most observers of this dynamic sequence describe affects as unfolding epigenetically and differentiating from earlier affects through the double prism of maturation and experience (Schmale 1964; Pine 1980). Transitions from one phase to another are never discrete. The process, though gradual, is a continuous one.

During the autistic phase, the infant's experience is closely tied to physiology and consists of states of tension alternating with states of quiescence or sleep. Although tension level is largely modulated by the mother, the infant has no awareness of this or of her as a separate object. That is, although normal autism is an object-related state, the infant is not aware of this relatedness at a psychological level. Any nascent sense of self (as mind and/or body) derives from sensate reality. That is, sensation may serve to focus attention and provide concrete definition to the body. This is the phenomenon of "adhesive identification" (Bick 1968; Meltzer 1974) in which the normal neonate in the autistic stage searches for "an object—a light, a voice, a smell, or other sensual object—which can hold the attention and thereby be experienced, momentarily at least, as holding the parts of the personality together" (Bick 1968, p. 484).

During the autistic phase, affects, when observed, are primitive and undifferentiated. Novey (1959) postulates that the infant experiences two monochromatic affects—pleasure and unpleasure. Tension or unpleasure in particular can crescendo rapidly into panic (organismic distress) and random motoric discharge if unrelieved.

Beginning in the autistic phase, the normal infant has a capacity to withdraw or habituate (i.e., to raise his threshold) to impinging inner and outer stimulation (Brazelton 1962; Wallerstein 1967). Additionally, mother modulates stimuli. In concert, this constitutes the stimulus barrier (Freud 1922; Bergman and Escalona 1949), which usually guarantees optimal levels of tension and which later may become part of the capacity for repression (Aleksandrowicz 1977). As such, the stimulus barrier provides the infant with his first adaptive and defensive coping mechanism. It involves complex neurophysiological processes of "conservation-withdrawal" which, as reviewed by Schmale (1973), are common to all biological organisms.

In the symbiotic phase mother and infant form an omnipotent system, a dual unity within one common boundary (Mahler 1968). At the same time, the infant's maturing cognitive apparatus turns attention increasingly beyond the symbiotic orbit to the external world and epistemophilic pursuits. By around 8 months, the resulting greater differentiation of boundaries leads to separation anxiety, usually manifest behaviorally by "low-key activity" when mother is absent. McDevitt (1979) postulates that during this state the child is preoccupied with an inner feeling of previous closeness with mother. That is, he regresses in fantasy to an earlier symbiotic union. To the observer this usually appears affectively "silent" (i.e., the infant simply withdraws from external orientation).

In general, the symbiotic phase is one in which affects appear in greater profusion and modulation. Longing and signal anxiety supersede panic. Anger more often replaces rage, and sadness enters the array, frequently tempering desperation. Psychically, affects accrue value or meaning (i.e., they become "good" or "bad"). With the greater differentiation of symbiotic self from nonsymbiotic self, the coping mechanisms of splitting and projective identification come more into play as mechanisms for the protection of the cohesive symbiotic self (which becomes idealized) by disavowing unpleasure beyond this orbit to "not-we" objects (which become devalued and/or persecutory).

The practicing stage of separation/individuation (9–16 months) sees the gradual emergence and consolidation of *mood*—more general affective states characterized by temporal spread (lasting over time) and spatial spread (coloring reactions to all stimuli) (Pine 1980). The now verbal and upright toddler practices with gusto. The exhilaration of effectualness (turning passive into active) fills the toddler with a sense of power seen as the basic mood of elation (Mahler 1966). This "magical" sense of omnipotence and safety, though partly deriving from newly self-generated capacities, also stems from its earlier source of the symbiosis. The sense of oneness with mother goes untested as long as she remains reliably close for periodic "refueling" and empathic contact.

During the rapprochment subphase of separation/individuation (16 months to 3 years), the toddler's imperviousness to frustration falters. His increasing capacity to realize his actual dependence, smallness, and separateness from mother challenges the older symbiotic delusions of omnipotence. He now reapproaches mother to woo, impress, or shadow her and reclaim the symbiosis and power which she is experienced as possessing but withholding (Mahler 1972). The child's elation and grandiose self-esteem are vulnerable to deflation, and the basic moods are often those of anger, sadness, or depression (Mahler 1961). Successful passage through this stage depends upon the graded titration of disappointments, allowing for concomitant reinvestment of interests and idealizations onto the newer, more reality oriented (alloplastic) ego functions.

During the fourth subphase of separation/individuation or object constancy (third and fourth years of life), solid differentiations of self- and object-images occur which integrate and contain both good and bad components. Mother is seen as a separate, whole person, reliable in her love, but capable of being frustrating as well. The affective state of mourning or grief requires the cognitive acquisition of object constancy (or the permanence of attachment) and the cognitive awareness of the permanence of loss (a concept of death) (Pine 1980) which is not usually attained fully until adolescence (Wolfenstein 1966).

Thus in the course of *normal* development the affect of depression as we usually define and empathically recognize it differentiates distinctively by the third subphase of separation/individuation. Joffee and Sandler (1965), like Bibring (1953), feel that depressive affect is a "fundamental psychobiological" response to the experience of helplessness in the face of persistent discrepancies between actual states of tension and an ideal state of satiation and power. They caution that below the surface phenomenology of depressive affect, however, one needs to distinguish the pathologic depressive response from the normal reaction of grief and mourning. Though the grieving individual may look depressed, intrapsychically he *faces* the painful loss and gradually accepts the real unattainability of the lost ideal state or object. This leads to recovery through reinvestment in new ideals and objects. The depressive response, however, entails passive capitulation to helplessness seen as an inhibition of function. The ideal state remains unmodified and unrelinquished but experienced as unattainable. According to Smith (1971), in depression the inevitability of loss and separation is denied. Grief signifies acknowledgment of "a particular loss in itself and the inevitability of loss in the achievement of separateness." (Smith 1971, p. 265).

As a transient response, depression may be followed by mourning and individuation, but it may also become established chronically as a defense. Given this, depression as so defined is not necessarily indicative either of individuation or of therapeutic progress. Thus we need to be cautious in identifying a depressive response as a positive prognostic sign. This is particularly true in the therapy of schizophrenia where depression frequently becomes reified not only as a good prognostic sign but also as a therapeutic goal in itself. It behooves us to look beyond phenomenology to the dynamics of a given clinical situation to differentiate depression as a pathological stalemate from maturational grief.

Affect in Childhood States of Stress and Psychopathology. Let us now shift to affect in childhood as described in states of stress and psychopathology. As noted, Novey (1959) postulated the existence of two primitive affects in the normal autistic phase—pleasure and unpleasure. He subdivided the latter into rage, primary anxiety, and aphanisis. Freud (1971) considered primary anxiety to be the traumatic state (of organismic panic) experienced by the helpless infant exposed to unrelenting discomfort. Following an initial rage response, primary anxiety ensues, and eventually the infant ceases to struggle. This cessation Ernest Jones (1929) termed "aphanisis."[1] In this earliest form of despair, the infant relinquishes expectation of comfort and avoids all stimulation through withdrawal. In the neonate, aphanisis is largely a physiological operation and seems to represent hypertrophy of the normal stimulus barrier.

Broucek (1979) recently described what might be termed an experimentally induced state of aphanisis in neonates and young infants. The operant conditioning experimental procedure produced multicolored stimulation from a blinking light whenever an infant rotated his head 30 degrees. Orientation reactions (i.e., learning) occurred rapidly and were accompanied by unmistakable "joyful affects." When the paradigm was manipulated so that the learned contingency relationships no longer held (i.e., the light no longer blinked), the infant increased his activity to discover a new contingency. If unsuccessful, there ensued a sudden and dramatic behavioral change described as a "biological playing possum." In this state:

> The infant lies motionless with nonconverging, staring eyes, and sleeplike respiration. This passive behavioral state, which may be characterized as a sort of total inner separation from the environment, may appear more frequently during the first two months than later on. In similar situations infants older than three months tend much more to avoid actively everything connected with the unsolvable problem. [Broucek 1979, p. 313]

Broucek noted that the motionless, nonconvergent, sleeplike, curled-up, passively withdrawn infant suggested an infantile catatonic state. Relevant here as well is the unresponsive, withdrawn state described by Engel and Schmale (1967) which ensued in the infant Monica when her cries of distress were ignored by her mother.

In psychopathological syndromes of autism and childhood psychosis, infants and children use a wide repertoire of defensive maneuvers, which, like aphanisis, appear to represent primitive forms of detachment from unpredictable internal and external stimulation (Anthony 1958; Mahler 1968; Kernberg 1979; Tustin 1980). Some maneuvers appear to be automatic or passive forms of avoidance or withdrawal, such as affective detachment (no voice modulation or social smile), deanimation, pseudo-deafness, visual evasion, or a raising of sensory and pain thresholds such that these children can bang or bite themselves with little obvious discomfort. Other mannerisms appear to be more active efforts to produce sensations or to order and focus attention in the service of obliterating intrusive and unpredictable stimuli. Such children create "a rigid system of idiosyncratic, sensation-dominated activities" (Tustin 1980, p. 27), such as body stiffness, sucking of the tongue, stereotypic muscular movements, and the meaningless perseveration of speech and words. Body and objects are used "autistically" (i.e., not for meaning or play but for their diversionary sensory value—such as hardness—in order to shut out unpleasure) (Tustin 1980). Such pathological augmentation of the stimulus barrier may be present at birth (primary autism) or reactive (as a "second skin") to early uncontrollable overstimulation (Anthony 1958).

It is generally agreed that such pathological states are presymbiotic (i.e., they represent failures to achieve significant symbiotic attachment in which the mother is allowed to participate in the process of stimulus modulation). When an infant has established symbiotic relatedness, stress appears to result in a different syndrome, which has been termed anaclitic depression. Spitz (1946, 1965), Bowlby (1960), and Bowlby, Robertson, and Rosenbluth (1952) describe the responses of symbiotic-phase infants (second half of the first year of life) to prolonged separation from their primary caring objects. Descriptions include protest, crying, sadness, rejection of the environment, and active withdrawal with inactivity. As such, these children demonstrate more recognizable precursors to what we ordinarily term as depression. In contrast to aphanisis and pathological autism, despondency and depressive mood are clearly present. Smith (1971) termed this "primary depression" and indicated its presence implies sufficient differentiation for ego boundaries to exist, even if the boundaries are those of the symbiotic unit.

To summarize, the normal affect or mood of depression gradually consolidates around the third subphase of separation/individuation—well past the establishment of symbiotic relatedness. Depression as a pathologic syndrome can be seen as early as the second half of the first year of life in infants who lose a caring object with whom they appear to have developed a symbiotic relationship. Depression as either a recognizable normal affect *or* pathologic syndrome has not been reported before 6 months of age. Instead, one sees states of primitive undifferentiated distress, aphanisis, and autistic withdrawal, which are distinct from depression both phenomenologically and structurally.

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[1] Aphanisis (ah-fan-i-sis): The term, according to Dorland's Medical Dictionary (1965), means the obliteration of sexuality (or drive). It derives from the Greek meaning "disappearance."

Discussion

Synthesis of Theoretical Considerations and Case Material. Comparing the clinical data with descriptions of affect in normal development and childhood psychopathology, I maintain that what often passes as depression in chronic schizophrenic patients represents a less structured, more primitive psychic state of autism or aphanisis. For Dorothy, Sam, and Bill, affects were vague, physiologic in nature, and experienced somatically or concretely as undifferentiated pleasure or unpleasure. Sitting with them as an empathic observer, I could not recognize the more modulated and differentiated affects of depression, such as sadness, guilt, helplessness, and hopelessness. Their affective states could shift rapidly and unpredictably from blankness to unpleasure. Each state appeared to be experienced by them as global, total, and timeless. That is, what they experienced in the here and now was to them how they had always felt in the past and how they would always feel in the future. The ideal state for them appeared to be the tension-free state of no-feeling, nothingness, or blankness. They seemed to have no experience or notion of a pleasurable tension state. Pleasure for them reduced to the absence of feeling since, for them, pleasure itself was probably experienced as *over*stimulating and therefore unpleasurable by virtue of its overwhelming nature.

Dorothy, Sam, and Bill used a repertoire of coping strategies designed to obliterate external and internal stimulation through massive cathectic withdrawal. This could be observed as a blanking out of thoughts, affects, memory, and perception through the omnipotent denial of nihilistic delusions and negative hallucinations. They deanimated object relations and rendered the interpersonal process psychologically lifeless. They minimized stimulation by reducing or routinizing daily activity and preferred the posture of lying or sitting motionless in a sea of silence.

Dorothy, Sam, and Bill also scotomatized perception by focusing attention onto narrow tunnels of external reality or internal thoughts and feelings in the service of blotting out everything else, especially spontaneous and unpredictable stimulation. Any sensation emanating from an object (the body-as-object or the mind-as-object) could be used: the bedsheets, an office chair, a radio, a book, words, thoughts, and especially body sensations (muscular and skin) and body functions (breathing).[2] This process of scotomatization seems like the phenomenon of adhesive identification described by Bick (1968). For Dorothy, Sam, and Bill, there was psychic awareness of vegetative existence but no awareness of a personal identity beyond the immediate sensate focus. Such focusing serves a dual purpose not only of defense (as mentioned) but also of providing a primitive identity or self, the establishment of which seems to be as fundamental as the avoidance of unpleasure. The observed ability of cold, wet sheet-pack restraints to calm some severely regressed and fragmented psychotic patients may work by highlighting awareness of the skin over the entire body, thereby providing a "sensate sense" of intact body ego.

The states that Dorothy, Sam, and Bill present resemble phenomenologically and structurally (but are not equivalent to) the affective states seen in the normal presymbiotic or autistic neonatal period of development (i.e., states predating differentiated affect and mood, especially those of elation and depression). The states they present furthermore seem to involve coping strategies that pathologically elevate the stimulus barrier, thus resembling states of childhood autism or aphanisis in which stimulation is controlled by avoidance, stereotypy, and the annihilation of the experience of relatedness. What Dorothy, Sam, and Bill present, then, is aphanisis or "blank depression," a psychic state in which all mental activity is geared toward eliminating awareness of need or satisfaction, pain, or pleasure. It is the original anhedonia. I prefer the term aphanisis to autism because it avoids confusion with the infantile or childhood syndrome. What is described here is a regressively defensive process seen in adult chronic schizophrenic patients and, as such, is not equivalent to normal or pathological infantile autism.

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[2] The most frequent object used by Dorothy, Sam, and Bill seemed to be the cigarette. If not regulated by hospital staff, they would chain smoke all day long. The cigarette seemed to be their autistic object (Tustin 1980) par excellence insofar as it combined stimulation of the respiratory mucous membranes and the function of breathing. Inhaling smoke may provide a more "internal" sense of adhesive identification (i.e., a primitive reassurance that an inside does exist).

Aphanisis in Chronic Schizophrenia: The Syndrome.

Aphanisis is often overlooked as a symptom complex because of the "quietness" of its symptoms. In appearance and behavior, patients often present a "wooden" exterior. They sit or lie quietly with unblinking, staring eyes. This is usually accompanied by motor inactivity or stereotypy. Patients are socially withdrawn, often requesting to spend time by themselves in their room or in bed. Concern for dress and grooming is titrated to the minimal expectations of the milieu. Eating and sleeping cycles may shift out of phase but in an erratic and unpredictable fashion. Strikingly, level of consciousness seems to be inappropriately out of phase with level of physical activity. That is, patients are wide awake yet immobile. When sitting with such patients, one often feels out of contact, stimulus deprived, and sleepy; yet no matter how bitterly such patients may complain about being tired, they do not respond to their inactivity and remoteness with drowsiness.

Patients in a state of aphanisis are alone, isolated, asocial, and interpersonally out of contact. They may be compliant to social role but remain unrelated in any spontaneous or meaningful way. They impart no sense of recognition of others as needed or powerful.

The mood or affect of such patients is striking in its absence. One is met by a great blandness and blankness. The patient seldom shows any emotion other than the primitive varieties described earlier. Tears of laughter or sadness are virtually nonexistent, but the bizarre facial contortions of silliness or horror can sometimes be observed.

Thought processes are largely intact and understandable, though often concrete. Repetitive thoughts are common. Thought content tends to be blank, sparse, and very private. Patients may report fatigue, neurasthenia, somatic preoccupations, or compulsive thoughts that are used for focusing (as described). Thoughts are not differentiated according to meaning; they are treated like objects. Suicidal thoughts, for example, are often present but seldom have meaning as intent. Dorothy, for example, experienced thoughts about killing herself every month for 5 years but never actually came close to trying. Instead, these thoughts, like objects, provided her with identity and focus. She was, in effect, able to define herself by saying, "Here I am, Dorothy, who is sitting here in Dr. McGlashan's office and thinking suicidal thoughts."

In the acute, fragmented, or florid phase of a schizophrenic psychosis, aphanisis is seldom seen except, perhaps, in severe catatonic stupors, especially those in which the patient (later) reports having feared moving or thinking lest his experienced world explode into pieces. In the postpsychotic phase of acute and subacute breakdown, aphanisis can be a relatively stable psychic state. As a long-term adaptation in the chronic patient, however, aphanisis can frequently oscillate with states or periods of fragmentation and more florid symptomatology (delusions, hallucinations, and thought disorder), as was the case with Sam and Bill. "Remission" from such regressions, however, usually means a return to the baseline of aphanisis.

Some other current descriptive terms for this state in chronic schizophrenia are: residual defect or deficiency symptoms of schizophrenia, the negative symptoms of schizophrenia, institutionalization syndrome, demoralization, burnout, and schizophrenic apathy. Most of these terms, I feel, are misleading because they imply a largely organic deterioration or deficit rather than a psychologically defensive distortion of function which, upon closer scrutiny, appears to account for *part* of the picture, at least. Structural and biological factors undoubtedly operate as well, but have too often been held as accounting for it all. As such, I prefer the term "aphanisis," which reemphasizes the role of conflict and defense in these otherwise "organic" appearing deficit states.

From a psychodynamic point of view, the sense of self refers to the degree of cohesiveness, organization, or continuity with which the self is experienced. In aphanisis, there is a conscious, fairly organized or coherent, stimulus or reality oriented self that is defined by adhesive identification in a physical body space in unidimensional time (an ever extending, immediate present). This self, however, is like a surface surrounding a "black hole" in psychological space. Present is the social role cohesiveness of Winnicott's (1965) false self but no inwardness, no sense of self "inside." In short: the "I" is present but blank. There is little awareness of inner tension and affect. It may be accompanied by the awareness of the absence of tension, usually reported as "feeling" empty or void inside or as perceiving the world in colorless, lifeless tones. To the empathic observer, the patient is experienced as a shell with a center missing, an object without interpersonal relatedness. This absence of empathic contact and recognition is so extreme as to be bizarre and uncanny and the patient is described as if he were dead, burned out, or zombie-like.

Motivation and purpose are not experienced except as efforts to maintain the status quo. As seen in the examples of Sam's meditation and Dorothy's compulsive thoughts, the self-coherence itself is "idealized" and "worked at" to maintain. This idealization, however, stems from an omnipotence which is autistic in nature. It should not be confused with the shared omnipotence of symbiosis. In aphanisis, idealizations pertain only to the experience of a cohesive and tension-free body self and do not include an idealized parental imago in Kohut's (1971) terms.

Aphanisis serves the autoplastic (internally adaptive) aim of maintaining self-cohesion through adhesive identification at the cost of the awareness of all affect, positive as well as negative. As such, it is nonadaptive alloplastically except as a holding action and always remains potentially fatal in a nonwelfare environment. Coping strategies involve the primitive and global defenses of obliteration and scotomatization. They result in a focusing on details of thoughts or perceptions as a way of restricting input and holding on to reality, organization, and cohesiveness (Pious 1961). A common mechanism underlying these defenses is horizontal splitting or the topographic splitting of the mind into conscious and unconscious. As such, aphanisis may constitute the most primitive form of what eventually differentiates into repression.

In aphanisis, gross ability to test the factual realities of immediate environment (time, place, and person) appears largely intact. Nevertheless, considering the degree to which affective experience is obliterated, concretized, or scotomatized, one might speculate that the patient's perception of reality is altered in the direction of appearing simple, concrete, flat, and void of complex personal meanings, such as causality, motivation, and relationship.

The psychic state of aphanisis corresponds to presymbiotic levels of object relationships. There is no separation anxiety because there is no recognition of loss of a prior relatedness. Like normally autistic infants, patients in this state require an auxiliary object or environment for survival, but they have no psychic awareness of this. Dorothy, Sam, and Bill, for example, were all convinced they could leave the hospital at any time despite the overwhelming magnitude of their respective disabilities. This also exemplifies their defective reality testing in the realm of "meaning" and "significance." They cannot test reality beyond the concrete and factual because to them there *is* no reality beyond the concrete and factual. People are not "personalities" with whom one has a "relationship"; they are objects essentially no different from inanimate objects with which one has a purely sensate relationship.

Other authors on the subject of schizophrenia have identified states which may resemble aphanisis. Bleuler (1950) described the common symptom of affective indifference in schizophrenia wherein the patient reports feeling dead. Fairbairn (1954) felt that the schizophrenic patient withdraws his libidinal investments to such a degree that all emotional ties with the object are removed, leading to the perception of the world as ghostly and meaningless. Van Dusen (1959) maintains that a central experience of the chronic schizophrenic patient involves an experience of "blankness or nothingness" described by some patients as a "dark hole," or as "selflessness, timelessness, and spacelessness." In this state the patient ceases to talk, looks "caught," and is silently desperate. Subjectively, Van Dusen speculates that the patient experiences the disappearance of the world and his identity as feelings drain from perception. Pao (1979, p. 157) notes that primitive "maintenance mechanisms" are reactivated at times in schizophrenia leading to a "temporary erasure of self and/or object representations—clinically resembling repression of a profound order," and seen in its most common form as an "absence" or "blocking."

There may exist some link between the state of aphanisis and the nonpsychotic syndrome of alexithymia recently described by Sifneos (1975) and Nemiah (1975, 1978). Common to patients with psychosomatic disorders, this syndrome is characterized (in part) by an inability to distinguish affects, to localize feelings in the body, or to describe feelings in words. There is an impoverishment of fantasy and a preoccupation with minute external situational details. During interviews the patients appear expressionless, stiff, wooden, and dull or boring to the interviewer. Nemiah (1975) hypothesizes that alexithymia may result from overinhibition of the impulse pathways from the limbic striatum to the neocortex (awareness). Considering acute schizophrenia to be an uncontrolled chaotic flooding of the neocortex with memories, sensations, and affects, he suggests that alexithymia and psychosomatic disorders may have an inverse relationship with schizophrenia. As such, the syndrome of aphanisis, which shares many clinical characteriestics with alexithymia, may represent a reactive overinhibition of these pathways to compensate for the disinhibited flooding of the acute psychotic breakdown.

Note on the relationship of aphanisis to antipsychotic medication. Recent observations leave little doubt that neuroleptic medication can induce extrapyramidal akinetic (Rifkin, Quitkin, and Klein 1975; Van Putten and May 1978) or pseudo-catatonic (Gelenberg and Mandel 1977; Brenner and Rheuban 1978) states which, though side effects, can mimic aphanisis in many of its features. These drug-related conditions can usually be identified by the observation of drowsiness, reversal with drug discontinuation, or rapid clinical response following the introduction of antiparkinsonian agents (Van Putten and May 1978; Van Putten, May, and Wilkins 1980). At the same time, however, the etiologic contribution of medication may not be limited to extrapyramidal side effects since Dorothy, Sam, and Bill presented pictures of aphanisis or pseudo-depression while receiving antiparkinsonian drugs. At the same time, medication was (to my mind) clearly involved. Drugs seemed to precipitate the syndrome in Dorothy, who before receiving neuroleptics, had remained unrelentingly fragmented and confused. For Sam and Bill, medication seemed to increase the frequency and length of times each spent in pseudo-depressive immobility. Although it is impossible to generalize from three cases, I would at least hypothesize that neuroleptic medication is connected with the state of aphanisis by some as yet unknown mechanism, perhaps by somehow rendering the outlined coping strategies more effective and resistant to regressive breakdown.

Differential diagnosis. At the current state of our knowledge, it appears that once a drug-related side effect has been ruled out, the differential diagnosis of postpsychotic depression in schizophrenia narrows to a choice between aphanisis, depression, and reactive grief.

In contrast to aphanisis, the clinical picture of postpsychotic *depression* is more typical of that which characterizes affective disorder. In appearance and behavior there is psychomotor retardation or agitation. Vegetative signs of energy loss, sleep disturbance, and shifts in weight and appetite follow more classical lines. The mood and affect are unmistakably recognizable and consist of palpable despondency, gloom, and pervasive sadness, sometimes accompanied by weeping.

The patient feels very related to others, although in a distorted way as the bad and helpless infant. Others are recognized to exist; they are viewed as all powerful and urgently needed. Such patients often cannot stand moments of separation, yet at the same time feel burdened by the task of relating. The patient's mode of relatedness to others elicits strong countertransferences—usually feelings of helplessness and impotence. The therapist therefore may feel uncomfortable but seldom experiences being out of contact with the patient.

Thought processes are largely intact, though usually slowed. In contrast to aphanisis, thought content in postpsychotic depression is often rich in material of a depressive nature. The patient complains of being incompetent, defective, or sinful. He feels guilty about being a burden or a danger to others and feels shame over past psychotic behavior. He complains of hopelessness and helplessness, anticipates failure, lacks self-confidence, and repetitively attests to his worthlessness. Suicidal ideas are common and need to be taken seriously. In contrast to aphanisis, they convey intent. Complaints of fatigue and lack of initiative (neurasthenia) and somatic preoccupations are common to both depression and aphanisis and therefore do not discriminate between them.

In depression, feelings of worthlessness may reach delusional proportion. Nevertheless, these are distinct from the nihilistic delusions of aphanisis. The depressed patient may feel worthless, but this means he possesses a psychic notion of *worthiness*. Nihilistic delusions, on the other hand, are "pre-worth." They involve no issue of good or bad (value); rather, the issue is one of sensation versus nothingness. In aphanisis there is no hopelessness because there is no concept of hope, and there is no helplessness because the only issue is one of being, not one of doing.

Postpsychotic *depression* is more likely to be seen in the less chronic schizophrenic and/or in those in whom episodic breakdowns are followed by good remissions. Such patients possess a healthier nonpsychotic part of the personality (Bion 1957) which is developmentally more advanced and therefore capable of depression or grief, that is, of *holding* a painful situation and of acknowledging the loss of the omnipotence of the psychosis—for example, MacKinnon's (1977) patient. In contrast, one sees a strengthening of omnipotent defenses in aphanisis.

Structurally and dynamically, aphanisis is presymbiotic and involves denial of any affective state, actual or ideal. In contrast, depression is symbiotic. An ideal state has psychic representation and is not denied, but the subject feels helpless in actuality and relinquishes active attempts to attain it. Hopes for passive rescue, however, remain viable. Denial occurs but involves denial of separateness from the ideal state. That is, the painful situation can be held in depression, but it cannot be let go because of overwhelming separation anxiety. Grief presupposes the successful negotiation of both symbiosis and separation/individuation. Hopelessness is transiently experienced but overcome through transformation of the ideal more in accord with reality. The individual retains confidence in his ability to attain a repaired or reconstructed ideal and does not feel an ultimate dependence upon rescue from an omnipotent object. Separateness and the inevitability of loss are not denied.

Prognostic and treatment implications. Careful differential diagnosis may provide more accurate prognostic estimates for any given case of "depression" in the postpsychotic state, with aphanisis predicting negatively, grief predicting positively, and depression being indeterminant. A word of caution is necessary here. Although aphanisis and depression may become maladaptive end responses to stress, they can also be transiently defensive. Thus, tolerance is required with every patient in hopes that progress will ensue upon exposure to therapeutic resources. By and large, aphanisis is a relatively stable, chronic state, although the phenomenon of late onset recovery in a significant subsample of chronic schizophrenic patients (Bleuler 1980) indicates that aphanisis is not irreversible.

More careful differential diagnosis may also aid in the process of choosing (or researching) treatment. Antidepressant medications, for example, may aid a truly depressive response but fail with aphanisis, and both antidepressants and neuroleptics may interfere with maturational grief (Schulz 1975).

The implications for psychotherapy (if psychotherapy is used) constitute another study in itself, and only brief speculations will be advanced. For aphanisis, the emphasis may focus on establishing symbiotic relatedness (Searles 1965)—a long and difficult process. To allow for the unfolding of affect within such a relationship takes time and patience. States of depression may often be approached with more classical "analytic" activity (i.e., confrontation and interpretation of depression's defensive functions). Finally, when grief appears predominant, interventions should support the ongoing mourning process and protect it from veering off into pathologic resolutions.

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Longitudinal, Prospective Evaluations of Intelligence in Children at Risk

by Julien Worland, David G. Weeks, Steven M. Weiner, and Judith Schechtman

Abstract

Data are presented from the intellectual assessment of 153 children at two test periods in the St. Louis Risk Research Project. At phase I (1967–72) the Wechsler tests of intelligence were administered to offspring in families with one schizophrenic parent, one parent with affective disorder, one parent with schizoaffective disorder, one physically ill parent, or to offspring with two normal parents (mean age, 8 years). At phase II (1975–78) the intelligence of offspring was tested again at a mean age of 16 years. Differences between children as a function of parental diagnoses were assessed using a repeated measures analysis of covariance. The analyses yielded significant time effects. A time-by-parental-diagnosis effect was found for Verbal IQ, with children of parents with schizophrenia, affective disorder, or physical illness all showing a greater decrease in their scores at the second testing than offspring in the other groups. Offspring of psychotic mothers had lower IQ scores than those of psychotic fathers. Children of schizophrenics and children of schizoaffectives had the lowest stability in IQ scores from the first to the second testing.

There is considerable evidence that adult schizophrenics suffer from a variety of cognitive deficits, not the least of which is an intellectual deficit (e.g., Pollack, Woerner, and Klein 1968), and that they suffer a deterioration in several components of intelligence after the onset of psychosis (Lubin, Gieseking, and Williams 1962).

Retrospective studies of the intellectual performance of children who later became psychotic adults have yielded evidence of early interference in the development of intelligence in future schizophrenics (Rappaport and Webb 1950; Lane and Albee 1964; Heath, Albee, and Lane 1965; Schaffner, Lane, and Albee 1967; Pollack, Woerner, and Klein 1970; Offord 1974). Despite some evidence to the contrary (Albee et al. 1963; Lane and Albee 1968), there is reason to conclude that intellectual deficit is an early concomitant of schizophrenia and is evident long before the emergence of adult illness (Lane and Albee 1964, 1965).

In the last 15 years, investigators have begun examining the intellectual development of children of schizophrenic parents because these children are at risk for the development of schizophrenia or for other kinds of emotional or cognitive pathology. Whether the IQ scores of the offspring of psychotic parents are lower than those of the offspring of nonpsychotics is not clear. Some investigators have reported that there are no IQ differences between the children of schizophrenics and the children of normals (Rutter 1966; Cohler et al. 1977; Rieder, Broman, and Rosenthal 1977; Worland and

Portions of this report were presented at the Plenary Conference of the High Risk Consortium, San Juan, Puerto Rico, March 11–13, 1980, and at the Annual Meeting of the American Psychological Association, Los Angeles, CA, August 24, 1981.

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Hesselbrock 1980); but others report that the children of psychotic parents do have lower IQ scores than children of nonpsychotic parents (Mednick and Schulsinger 1968; Landau et al. 1972).

Although not unequivocal, the results of past research suggest that the development of schizophrenia involves some degree of intellectual deterioration and that children of schizophrenic parents may be at risk not only for the development of psychosis but also for difficulties in the development of intelligence. Intellectual decline over time in a group of children at risk could indicate a disruption of cognitive development in a subsample of the children, and could be a warning signal for the beginning of a disease process to culminate later in recognizable adult psychosis. Thus, to understand the intelligence of children at risk from a developmental perspective is very important.

The purpose of the present study was to provide followup IQ data on a retested sample of offspring in the St. Louis Risk Research Project, from which comparisons of the IQs of children of normal, physically ill, manic-depressive, and schizophrenic parents were previously presented (Worland and Hesselbrock 1980), testing the following hypotheses: (1) Because we previously found no differences in IQ scores between the children of psychotic and the children of nonpsychotic parents, we hypothesized that the IQ scores of the offspring of psychotics would be no lower than those of the offspring of nonpsychotics when the followup data were considered. (2) We also hoped to determine whether our previously reported finding, that children of ill mothers had lower IQ scores than children of ill fathers, would remain true after an interval of from 6 to 10 years. (3) We also hypothesized that intelligence would be less stable over time for the children of psychotic parents than for the children of nonpsychotic parents. We made the third prediction because of the expected disruptive effects of emerging psychosis in a subsample of each of the risk groups.

Method

Subjects. The index parents were 22 psychiatric patients, described below, 15 physically ill parents, and 30 normal, nonhospitalized couples. These parents had 153 offspring of whom 10 were children of a schizophrenic parent, 20 were children of a parent with affective disorder, 17 had a parent with a schizoaffective disorder, 31 were children of a physically ill parent, and 75 were children of two parents with neither psychiatric hospitalizations nor prolonged hospitalizations for physical illness. Children were an average of 7.9 years when tested the first time, and averaged 15.6 years old at the second testing. Demographic statistics are in table 1. Details about their families and the procedures involved in securing the participation of the families have been presented frequently elsewhere, and will not be repeated here to conserve space. (For more details, see Anthony 1968; Janes,

Table 1. Demographic characteristics of children and families

Characteristics of children	Index parent diagnostic group[1]				
	SZ	AD	SZAF	PI	C
n	10	20	17	31	75
Sex					
Male	9	10	7	16	42
Female	1	10	10	15	33
Race					
White	10	7	12	14	52
Black	0	13	5	17	23
Age (months)					
Mean, time 1	96.40	108.50	86.56	88.40	95.37
Mean, time 2	186.00	204.85	173.17	193.47	183.40
Characteristics of families					
SES[2]					
Mean, time 1	28.00	39.25	29.59	48.58	27.55
Mean, time 2	39.30	39.70	37.65	50.71	27.15
Ill parent					
Father	8	8	4	18	—
Mother	2	12	13	13	—

[1] SZ = schizophrenia; AD = Affective disorder; SZAF = schizoaffective disorder; PI = physical illness; C = control.

[2] Hollingshead (1968) two-factor index of social position: Class I, 11–17; Class II, 18–27; Class III, 28–43; Class IV, 44–60; Class V, 61–77.

Hesselbrock, and Stern 1978; Worland, Lander, and Hesselbrock 1979; Worland, Janes, and Anthony 1980.)

Parental Diagnosis. To determine the parental diagnoses, one author (JW) read each psychotic parent's hospital index admission and discharge report, which had been edited to delete the hospital diagnoses and therapy regimens, and then made a *DSM–III* diagnosis (American Psychiatric Association 1980) for each case. We had hospital records for 22 of 32 index parents that allowed for a psychotic diagnosis using *DSM–III* criteria. Eighteen offspring of the 10 remaining cases were not used for these analyses. Because the 22 diagnosed cases represented a broad range of diagnoses, we grouped them into similar types for analysis. The *DSM–III* diagnoses, the groups into which they were aggregated, and number of offspring are presented in table 2.

Table 2. Parental diagnoses, number of families and children, and groupings for analyses

	n	
Group and *DSM-III* diagnosis	**Families**	**Children**
Children of schizophrenics (CSZ)		
1. Schizophrenic Disorder, Paranoid Type	1	2
2. Schizophrenic Disorder, Residual Type	1	1
3. Schizophreniform Disorder	1	3
4. Acute Paranoid Disorder, Paranoid Disorder	2	4
Children of affective disorder (CAD)		
5. Major Depression with Melancholia	2	6
6. Major Depressive Disorder, Single Episode	1	3
7. Bipolar Disorder	4	10
8. Atypical Depression	1	1
Children of schizoaffectives (CSZAF)		
9. Major Depression with Psychotic Features: Schizoaffective Disorder	6	10
10. Atypical Psychosis	3	8
Children of physically ill parents	15	31
Children of control parents	30	75

Testing. The intelligence tests were administered individually for the first time to this sample between 1967 and 1972, during or shortly after the ill parent's hospitalization. We again tested offspring between 1975 and 1978. The tests used were the Wechsler Preschool and Primary Scale of Intelligence (WPPSI; Wechsler 1967) and the Wechsler Intelligence Scale for Children (WISC; Wechsler 1949) at the first assessment, and the Wechsler Intelligence Scale for Children–Revised (WISC–R; Wechsler 1974) and the Wechsler Adult Intelligence Scale (WAIS; Wechsler 1955) at the second assessment, according to the age of the child. Tests were scored using the standard instructions. Eleven subscales were administered, including Digit Span but excluding Mazes on the WISC and WISC–R.

Design of the Analyses. The main analysis reported here is based on the two testings of the offspring, using a repeated measures analysis of covariance (ANCOVA), with parental diagnostic status used as the main effect, with socioeconomic status (SES; Hollingshead 1968) at each testing used as covariates, and Verbal IQ (VIQ), Performance IQ (PIQ), and Full Scale IQ (FSIQ) treated as dependent variables. We computed three additional ANCOVAs that included the sex of the ill parent as a factor, deleting children of normal parents.

Results

Parental Diagnosis. The ANCOVA for VIQ yielded a significant time effect, $F = 12.81$, $df = 1{,}147$, $p < .0005$, and a significant time × parental diagnosis interaction effect, $F = 2.97$, $df = 4{,}147$, $p = .0213$. There were also highly significant time effects for PIQ, $F = 6.98$, $df = 1{,}146$, $p < .0091$; and for FSIQ, $F = 15.52$, $df = 1{,}151$, $p < .0001$. Main effects for parental diagnosis were not significant for any of the three dependent variables.

The significant time × parental diagnosis interaction effect for VIQ can be explained by noting that children of schizophrenics, children of parents with affective disorder, and children of physically ill parents all showed decreases in VIQ scores from the first to the second testing, while children of parents with schizoaffective disorders and children of normal parents had virtually no change in VIQ scores between the two testings (table 3).

Table 3. Group means for IQ measures at phase I and phase II, by parental diagnostic status, adjusted for socioeconomic status

	VIQ		PIQ		FSIQ	
Group	**1**	**2**	**1**	**2**	**1**	**2**
CSZ	109.52	105.19	113.27	108.55	112.45	107.30
CAD	102.97	98.85	104.84	101.96	103.93	100.01
CSZAF	101.18	100.37	102.54	103.74	101.86	101.64
CPI	106.87	101.00	104.40	101.88	104.52	99.81
CN	109.06	109.30	110.10	108.39	110.53	109.74

Note. VIQ, verbal IQ; PIQ, performance IQ; FSIQ, full scale IQ; CSZ, children of schizophrenics; CAD, children of parents with affective disorder; CSZAF, children of schizoaffectives; CPI, children of physically ill parents; CN, children of normals.

Sex of Ill Parent. The main effects in the ANCOVAs for parental diagnostic group and sex of ill parent were not significant, for VIQ, PIQ, or FSIQ. However, diagnosis × sex of ill parent interactions were significant for VIQ, $F = 6.89$, $df = 3{,}69$, $p = .0004$; for PIQ, $F = 3.80$, $df = 3.69$, $p = .014$; and for FSIQ, $F = 4.36$, $df = 3, 73$, $p = .007$. The source of this interaction can be seen in the table of adjusted means (table 4). For all three psychotic groups, children of ill mothers had lower scores than children of ill fathers, but the reverse was true for the children of physically ill parents. The three-way interaction, time × sex of ill parent × diagnosis, was nonsignificant for all three dependent variables.

Stability of Intelligence. To test the hypothesis that intelligence would be less stable in the children of psychotics than in the children of nonpsychotics, stability coefficients were calculated separately for each diagnostic group, for VIQ, PIQ, and FSIQ. The stability coefficient in this case is simply the correlation between a test at the first testing and the same test at the second occasion. These correlations are presented in table 5. All the correlations were significant for children of parents with affective disorder, children of physically ill parents, and for children of normal parents. However, intelligence scores were clearly less stable for children of schizophrenics and children of schizoaffectives; for each of these two groups, one of their three correlation coefficients was not statistically significant.

Discussion

As we hypothesized, we could find no difference in IQ scores between children of psychotic and nonpsychotic parents, although we did find that children of schizophrenics, children of parents with affective disorder, and children of physically ill parents all had more loss in VIQ scores between the first and second testing than did the children of schizoaffectives and children of normal parents. We had not predicted this finding. There has been considerable previous evidence that children of schizophrenics may have lower IQ scores than those of matched controls. For example,

Table 4. IQ score means, adjusted for SES, for children of psychiatrically and physically ill parents, by sex of the ill parent

	CSZ		CAD		CSZAF		CPI	
IQ	**Father (8)**	**Mother (2)**	**Father (8)**	**Mother (12)**	**Father (4)**	**Mother (13)**	**Father (17)**	**Mother (13)**
VIQ1	111.87	101.70	107.60	97.36	105.18	100.03	95.40	114.07
VIQ2	103.40	104.70	104.86	92.19	105.31	97.21	89.20	107.83
PIQ1	113.38	111.99	111.30	97.91	107.31	100.60	95.15	109.57
PIQ2	108.47	100.98	110.80	93.36	101.07	102.77	94.78	103.86
FSIQ1	113.81	107.92	110.57	97.03	106.50	100.37	95.32	109.71
FSIQ2	106.40	103.42	107.94	92.13	103.20	99.52	90.31	104.62

Note. CSZ, children of schizophrenics; CAD, children of parents with affective disorder; CSZAF, children of schizoaffectives; CPI, children of physically ill parents.

Table 5. Time 1/time 2 correlations of intelligence measures, by group

Group	VIQ	PIQ	FSIQ
CSZ (10)	.519*	.310	.563*
CAD (20)	.849***	.855***	.872***
CSZAF (17)	.330	.446**	.471**
CPI (31)	.760***	.740***	.843***
CN (75)	.809***	.715***	.838***

Note. CSZ, children of schizophrenics; CAD, children of affective disorders; CSZAF, children of schizoaffectives; CPI, children of physically ill; CN, children of normals.

* $p < .05$.

** $p < .025$.

*** $p < .005$.

Watt, Grubb, and Erlenmeyer-Kimling (1980) found lower IQ in the offspring of one schizophrenic parent compared with the offspring of parents selected to control for socioeconomic status. Their findings, as well as those of Weintraub and Neale (1980) and those reported by Mednick and Schulsinger (1968), provide evidence that parental schizophrenia may be associated with slightly diminished offspring IQ. As yet, however, none of the investigators who have reported lower IQ scores in children of schizophrenics have used *DSM–III* criteria for the parents' diagnoses, and none of them have reported whether the observed differences could have been a function of the sex of the psychotic parent. Consequently, the issue must remain unsettled until replicated studies using *DSM–III* criteria and testing for effects of sex of the ill parent finally provide evidence that allows for a resolution of the matter.

When we compared the IQ scores of the offspring of ill fathers with those of the offspring of ill mothers, we were unable to replicate our previous finding that the offspring of ill mothers had lower IQ scores than the offspring of ill fathers, regardless of whether the parent was hospitalized for psychosis or physical illness (Worland and Hesselbrock 1980). Unlike our previous report in which we had found no interactional effect between parental diagnosis and sex of the ill parent, we found in the longitudinal analysis that the offspring with the lowest IQ scores were children of psychotic ill mothers and physically ill fathers. This provides evidence that the effect of parental psychosis on offspring intelligence may depend upon whether it is the father or the mother who is psychotic. Previous reports that have yielded lower IQ scores in the offspring of schizophrenic parents have either studied samples exclusively composed of the offspring of psychotic mothers (Mednick and Schulsinger 1968) or samples with a greater number of offspring of ill mothers than ill fathers (e.g., Erlenmeyer-Kimling's sample, from which the data reported by Watt, Grubb, and Erlenmeyer-Kimling, 1980, were drawn), or report no information on the sex of the ill parents whose offspring are studied (e.g., Landau et al. 1972). Further efforts to understand the effects of parental psychosis on offspring intelligence should therefore include information on whether the mother or the father was the ill parent.

Our final hypothesis was partially substantiated. The stability of IQ scores was far greater in the two nonpsychotic control groups than in the psychotic groups, with the exception of the stability for children of parents with affective disorder, who had the highest time 1/time 2 correlations. If replicated, this pattern would indicate that parental schizophrenic symptoms are associated with less stability in measures of offspring intelligence than parental affective symptoms. It still remains to be demonstrated that a lack of stability in these measures is associated with disturbance or emerging psychosis.

The stability coefficients might be challenged because of the small number of offspring involved in the analyses. We found large time 1/time 2 IQ correlations in those groups with large *n*'s, so it could be argued that the differences between correlations in the samples reflect greater sampling variability in the smaller groups rather than actual differences in the population correlations. In response to this suggestion, we note that the difference in *n* between the children of parents with affective disorder and the children of parents with schizoaffective illness (20 vs. 17) could hardly be the explanation for the enormous difference in the reported correlations in these two samples (.872 vs. .471 for FSIQ). Consequently we consider it unlikely that these correlations are simply a reflection of different sample *n*'s, and consider it more likely that the obtained correlations reflect real differences in the long-term stability of measures of intelligence in these samples.

Conclusions

This study warrants the following conclusions subject to the caution that the *n*'s for the analyses are somewhat smaller than desirable. First, offspring of *DSM-III*-defined schizophrenic, depressed, and schizoaffective parents do not differ from one another or from control offspring in IQ when social class effects are controlled. Second, over the long term, offspring of mentally ill mothers may have continuing deficits in measures of their intelligence, when compared to the offspring of mentally ill fathers. Finally, the offspring of schizophrenic and schizoaffective parents have less stability in measures of their intelligence than the offspring of affective disordered parents, physically ill parents, or normal parents.

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Schizophrenia-Related Grants and Contracts—Fiscal Year 1980

The National Institute of Mental Health (NIMH) administers the Federal Government's major program of support for research in mental health. NIMH conducts and supports research into the etiology, treatment, and prevention of mental and emotional illnesses and research on many public health problems related to mental health. The many biological, genetic, psychological, social, and environmental factors which affect and shape mental health and mental illness are studied through NIMH-supported research in hospitals, universities, mental health centers, and community settings.

The research, services, and training grants and contracts that appear below were selected for inclusion here on the basis of their direct relevance to schizophrenia. Each grant or contract has been categorized under the administrative component of NIMH that is involved with its funding and monitoring: the Division of Biometry and Epidemiology, the Division of Extramural Research Programs, the Division of Manpower and Training Programs, the Division of Mental Health Service Programs, the Division of Special Mental Health Programs, Office of the Administrator, Alcohol, Drug Abuse, and Mental Health Administration, and the Office of Program Development and Analysis.

Division of Biometry and Epidemiology

Measures of Untreated Psychiatric Disorders
MH 10328; $126,121

Dohrenwend, Bruce P.
Columbia University
New York, NY

This project involves an investigation into the relationship between poverty, social class, social mobility, and schizophrenia. The subjects are white Anglo-Saxon Protestants, Jews, Irish, blacks, and Puerto Ricans, some convicts, and mental patients who reside in New York City. In a second phase of the study, a newly developed interview instrument is tested and calibrated with a sample of 200 New York adults. The extent to which the instrument can be administered by lay interviewers who are not clinicians is examined.

In 1979, the focus is still on the newly developed Psychiatric Epidemiology Research Interview (PERI), an instrument designed to screen functional psychiatric disorders, independently of treatment status, in a demographically complex urban population. The PERI scales are calibrated through interviews with 600 adults from the general population and 500 psychiatric patients.

Hospitalization of the Chronic Mentally Ill
MH 34743; $103,346

Hargreaves, William A.
University of California, Langley Porter Neuropsychiatric Institute
San Francisco, CA

Three community mental health centers are studied with regard to their effectiveness in minimizing hospitalization, and the general restrictiveness of care for the chronically mentally ill. The following measures are developed: amount and types of mental health service capacity devoted to the chronically mentally ill through the public mental health system in a catchment area; degree of community orientation, as distinct from hospital orientation, of these service capacities; service utilization; service cost; and quality of interagency linkage or case management functions. These measures are related to measures of hospitalization and restrictiveness of care, which have been adjusted to take into account patient risk factors, such as premorbid social adjustment, marital status, age of onset, employment, previous hospitalization, and medication. The community mental health centers participating in this study are District Five Mental Health Center, San Francisco, California; Peninsula Hospital Community Mental Health Center, Burlingame, California; and Marin County Community Mental Health Services, San Rafael, California.

Hospitalized Mental Disorder in Quebec and Israel
MH 32430; $600

Lasry, Jean-Claude
Jewish General Hospital
Montreal, Canada

The relationships between ethnic and class stratification and rates of first psychiatric hospitalization are studied in Jewish ethnic groups in Israel and the Montreal area of Quebec. The major hypothesis, relevant to stress/selection issues in the etiology of schizophrenia, is that disadvantaged ethnic groups have higher rates of first hospitalization for schizophrenia at controlled levels of social class than advantaged ethnic groups. Secondary hypotheses relate to the relationship of immigration to the rate of schizophrenia and suggested differences in rates of affective psychosis between Ashkenazic and Sephardic Jews.

Use of Primary Care by Children Under Psychiatric Care
MH 33646; $120,170

Starfield, Barbara H.
Johns Hopkins University
Baltimore, MD

Relationships between use of primary care medical services and use of mental health services are studied in children, under 18 years of age, continuously enrolled in an organized health setting for at least 6 years. Major aspects of the project involve the degree to which there is constancy of utilization patterns over time (high users remaining high users and low users remaining low users), the degree to which patterns of use can be explained by morbidity (both psychosocial and biological), the association of patterns of use and type of use and demographic characteristics of the child and family, and the extent to which patterns of use (psychiatric and nonpsychiatric) cluster in families.

Epidemiology of Schizophrenia in Croatians
MH 34159; $9,415

Torrey, E. Fuller
Saint Elizabeths Hospital
Washington, DC

Prevalence rates for schizophrenia and manic-depressive psychosis are studied among immigrants who have settled in Minnesota. Data are compared with the rates for other immigrant groups in Minnesota and with rates for native-born Americans. Immigrant groups from high prevalence Croatian areas are compared with immigrant groups from the rest of Croatia. In addition, a case register in Zagreb, Yugoslavia, is examined in order to compare immigrants with individuals who remained in Croatia. The research is designed to provide data relevant to the basic question of genetic versus environmental causation of schizophrenia. The Croatian Fraternal Union in Pittsburgh, Pennsylvania is a performance site for this research.

An Epidemiological Study of Atypical Schizophrenia
MH 31673; $255,619

Tsuang, Ming T.
University of Iowa
Iowa City, IA

A population of approximately 300 patients admitted to the Iowa Psychiatric Hospital between the years 1934 and 1944 are followed under the same methods used for the longitudinal followup of patients involved in an ongoing study known as the "Iowa 500." The subjects are regarded as atypical schizophrenics, because they did not meet the rigid criteria used for the "Iowa 500" study. Controls are 160 surgical patients. The primary goal is to develop new specific criteria for subclassifying the major psychoses.

Division of Extramural Research Programs

Receptor Modification in Treatment of Tardive Dyskinesia
MH 28892; $54,452

Alpert, Murray
New York University Medical

Center
New York, NY

Clinical trials of L–dopa are carried out in schizophrenic inpatients concurrently suffering from tardive dyskinesia. It is postulated that tardive dyskinesia, which can occur after long-term treatment with neuroleptic drugs, results from a receptor supersensitivity to dopamine produced by long-term blockage of postsynaptic receptors by these drugs. It is hoped that these receptors will adapt to L–dopa, which increases central dopamine, after the initial worsening of the dyskinesia by this treatment, and that the L–dopa treatment can be terminated with the receptor sensitivity brought down to normal. The treatment sample is screened and characterized by treatment with physostigmine, a cholinergic agonist, during the baseline period.

In 1980, a double-blind crossover study is conducted to confirm results obtained in the clinical trials.

Language Perception and Production in Psychosis
MH 31593; $75,480

Andreasen, Nancy C.
University of Iowa
Iowa City, IA

The primary goals of this investigation are to determine the extent of language abnormalities in mania and schizophrenia, to map them functionally, and to assess them longitudinally. The investigation is concerned with studying both language perception and language production. The language perception component focuses on both syntactical and semantic processing. The language production component focuses on examining pragmatic aspects of language production with three methods: a rating scale developed by the investigator which assesses severity and type of language disorder, linguistic approaches which emphasize reference and cohesion, and a computerized taxonomic approach. The psychotic disorders studied are mania, schizoaffective disorder, paranoid schizophrenia, and hebephrenic schizophrenia.

Models of the Pharmacotherapy of Schizophrenia
MH 00238; $38,880

Antelman, Seymour M.
University of Pittsburgh
Pittsburgh, PA

Animal models are developed to predict which drugs will have potential for treatment of schizophrenia or may induce tardive dyskinesia. Brain sites involved in therapeutic and extrapyramidal drug action and in aspects of the disease are investigated. The effects of chronic systemic administration of antipsychotic agents on self-stimulation behavior are examined in rats with electrodes implanted in several dopaminergic brain sites.

A Stress Model of Amphetamine Psychosis
MH 24114; $91,694

Antelman, Seymour M.
University of Pittsburgh
Pittsburgh, PA

The role of norepinephrine and dopamine in brain self-stimulating behavior is evaluated. The possible role of these neurohumors in mediating neural events and drives is examined, using specific brain lesions and drugs which selectively deplete the neurotransmitters. Some studies are carried out on young rats to evaluate the effects of early chronic depletion of brain catecholamines on later self-stimulation behavior and basic drives. Interactions between norepinephrine and dopamine systems in regulating these behaviors are studied as well.

Subsequent studies investigate the effects of repeated stress or amphetamine administration on brain dopamine functions and sensitization of behavioral responses as a model of amphetamine psychosis or paranoid schizophrenia.

Models of the Pharmacotherapy of Schizophrenia
MH 32306; $42,913

Antelman, Seymour M.
University of Pittsburgh
Pittsburgh, PA

Animal models are developed to screen neuroleptic compounds for antipsychotic activity and induction of tardive dyskinesia. The effects of these drugs on electrical self-stimulation in rats with electrodes implanted in various dopaminergic areas of the brain are determined after acute or chronic drug administration or with drug withdrawal.

Synaptic Transmission in the Central Nervous System
MH 47370; $39,010

Baldessarini, Ross J.
Harvard University
Boston, MA

The investigator is studying the role of biogenic amines as central neurotransmitters in rabbits and rats. Specifically, he is using model systems describing the release and uptake of norepinephrine and related catecholamines to investigate other psychoactive substances, including histamine and serotonin. He is also studying altered amine metabolism as a possible mechanism of action of electroshock as applied in the treatment of depression. The role of abnormal amine metabolism and the release of false or abnormal central neurotransmitters as a mechanism underlying hepatic encephalopathy is also examined. Studies are conducted on the relationship of abnormal methylation of central biogenic amines to schizophrenia, assaying the blood of schizophrenics for abnormal amine metabolites. The long-range goal of this research is to provide developmental knowledge leading to a better understanding of the biology of psychiatric and neurological problems. Additional studies of dopamine are concerned with regulation of dopamine release and synthesis, and with the effects of neuroleptics on synaptic membranes. The supersensitivity of dopamine receptors induced by antipsychotic drugs, and the influence of this treatment on animal behavior is investigated as a model for human neurological side effects associated with chronic use of antipsychotic drugs.

Neuroregulators and Behavior MH 23861; $553,637

Barchas, Jack D.
Stanford University
Stanford, CA

The relationship between the biochemical mechanisms controlling the formation and action of the biogenic amines and brain peptides, and animal and human behavior, is the central theme of this interdisciplinary program project. The five project sections are:

Biochemical Regulation: Investigation is made of the mechanisms involved in the regulation of biogenic amine synthesis, including genetic differences in enzyme activity, synaptosomal synthesis, the role of pteridine in amine synthesis, and tyrosine and tryptophan hydroxylase activity. An epinephrine-forming enzyme in human and animal brains is characterized; catecholamine pathways are mapped; and the role of transmethylation in the biochemistry of schizophrenia is investigated.

Analytic Procedures: New procedures are developed for simultaneous assays or microassays in various tissues for the biogenic amines and their metabolites, and for triptolines, enkephalins, and lithium. Qualitative and quantitative analytical techniques as well as histochemical techniques are utilized.

Endocrine Processes: Hormonal roles of biogenic amines are investigated. The interrelations of adrenal medulla catecholamines to patterns of pituitary secretion are studied in psychiatric patients. Baseline parameters for melatonin secretion from the pineal gland, concentrating on circadian changes and episodic secretions, are established in normal individuals and extended to psychiatric patients. Kinetic properties of epinephrine release in normal subjects and in psychiatric patients are also investigated.

Behavioral Neurochemistry and Pharmacology: Chemical changes which accompany behavioral states are investigated in animals. The effects of severe chronic stress on the capacity of the catecholaminergic system to respond to stress are studied. Techniques for studying synaptic activity in intact preparations are explored. The underlying neurochemistry of drug-induced behaviors, such as hyperactivity, and natural behaviors, such as sleep, are examined. The physiological and pharmacological properties of the enkephalins are studied in relation to pain pathways and environmental and physiological modulators.

Clinical Processes: Social and psychological influences on endocrine function are investigated in normal individuals, focusing on changes in catecholamine secretion with acquired social status. Metabolic differences in central neurotransmitter and neuroendocrine function are investigated in schizophrenic, autistic, and depressed patients and in control subjects before and after drug therapy. Enzyme changes in brain autopsy material from schizophrenics are also examined.

In 1981, the investigation of the relationships of neuroregulators to various mental diseases continues, with an analytical and histochemical approach which interfaces with the clinical program. The significance of the opioid peptides, catecholamines, and indoleamines is explored in the various biochemical/behavioral domains. Analysis procedures such as high pressure liquid chromatography, molecular genetics, and mass fragmentography are used.

Neuroregulatory Agents and Behavior
MH 24161; $39,107

Barchas, Jack D.
Stanford University
Stanford, CA

The interactions of neurotransmitter and neuromodulator substances, including catecholamines, indolamines, γ-aminobutyric acid, acetylcholine, and endogenous opiate-like peptides, with brain function in the regulation of behavior are investigated in a series of animal and human studies. The mechanisms of biochemical regulation and neuroregulator formation, including genetic regulation, are studied and assay techniques are developed and improved for these enzyme systems and neuroregulators. Behavioral neurochemistry studies in animals include examination of pineal function; sleep and narcolepsy studies in dogs; the effects of amphetamines on social behavior and as a model for paranoia in monkeys; and changes in enkephalin and endorphin levels in specific brain areas of rats following stress situations.

Clinical studies examine naltrexone treatment and endogenous opiate levels in schizophrenia; the role of cholinergic mechanisms in schizophrenia, manic psychosis, Huntington's chorea, and tardive dyskinesia; biochemical and biological correlates and neurotransmitter metabolism and schizophrenia and depression; pituitary/adrenal function in depressed patients in relation to neuroregulator function; and status alterations in small groups in terms of endocrine function and catecholamine metabolism.

Neuromelanin, Chlorpromazine and Tardive Dyskinesia
MH 33946; $37,672

Barden, Herbert
New York State Psychiatric Institute
New York, NY

Histochemical changes in neuromelanin and related compounds are characterized in human postmortem brain tissue from chlorpromazine-treated patients with or without tardive dyskinesia.

Genetics of Schizophrenia
MH 00176; $48,099

Baron, Miron
Columbia University
New York, NY

Two studies relating to the genetics of schizophrenia are performed. The objectives of the first study are to define a spectrum of psychopathological states related to schizophrenia, and to specify modes of transmission derived and tested according to principles of quantitative genetics. Multiple threshold models of inheritance are applied to data collected from first-degree relatives and spouses of schizophrenic patients and from control subjects. The objective of the second study is to test platelet monoamine oxidase as a genetic marker for vulnerability to schizophrenia, and to assess its relevance to genetic threshold determination.

Genetics of Schizophrenia
MH 30608; $108,910

Baron, Miron
New York State Psychiatric Institute
New York, NY

Schizophrenic subjects, normal control subjects, spouses, and first-degree relatives are studied in order to define a spectrum of psychopathological states according to the principles of quantitative genetics. A second study tests platelet monoamine oxidase (MAO) in schizophrenic subjects from the first study and a new sample of control subjects. The hypothesis of the second study is that MAO is a genetic marker for vulnerability to schizophrenia.

Social Skills Training for Day Hospital Schizophrenics
MH 32182; $94,935

Bellack, Alan S.
University of Pittsburgh
Pittsburgh, PA

The effects of adding a social skills approach to the standard day hospital treatment program for chronic schizophrenic patients are evaluated. Schizophrenic patients are assigned to three subject groups. One group receives the usual day hospital care. The second group receives that care plus three 60-minute periods of skills training, and the third group receives the usual day hospital care, two 60-minute periods of skills training, and two afternoons of practice of these skills in the community. After treatment, each of the groups is followed up at 3-, 6-, and 12-month intervals, with half of the subjects in each group receiving booster treatment once a month for 6 months. The social skills approach is based on the conception that effective interpersonal behavior is substantially a function of the individual's repertoire of learned response capabilities or skills. Patients are taught conversational skills, assertion, and skills to solve daily problems in living by means of direct instruction, role playing, feedback, positive social reinforcement, and modeling. Training in improved social perception is included.

Diagnosis Using Structural Analysis of Social Behavior
MH 33604; $121,726

Benjamin, Lorna S.
University of Wisconsin
Madison, WI

The possibility of more systematically incorporating psychosocial behavior into traditional psychiatric nosology is examined. In addition, a new classification of persons, which is based on interpersonal behavior, is in the process of development. The research involves analysis of subjective (by self) and objective (by others) ratings of interpersonal behavior and psychiatric symptoms for psychiatric inpatients and outpatients in different diagnostic categories.

Orienting Response Excess and Asymmetry in Chronic Schizophrenia
MH 28594; $89,750

Bernstein, Alvin S.
Downstate Medical Center
Brooklyn, NY

Attentional factors in schizophrenia are investigated. Physiological measures considered to constitute an orienting response to novel stimuli are utilized as the index of attention. The focus of the study is on habituation, or the elimination of the orienting response as a result of a continuous exposure to the stimulus which evoked it. The possibility that schizophrenics may display overly rapid habituation followed by overly rapid dishabituation—reappearance of the orienting response—is examined. If it is found that schizophrenics do display this phenomenon, electroencephalographic measures are studied to determine if this dishabituation represents a special schizophrenic property for the release of subcortical centers from higher control, or if it is the result of rapid increases in arousal. The investigator is also following up on preliminary indications that the orienting response in schizophrenics shows bilateral asymmetry. Subjects are schizophrenics, nonschizophrenic psychiatric patients, and normal individuals. The Kings County Hospital Center in Brooklyn, New York, is a performance site for this research.

Brain Tissue Resource for Neuropsychiatric Research
MH 31862; $160,443

Bird, Edward D.
McLean Hospital
Belmont, MA

A collection and distribution center for brain specimens obtained at autopsy from patients with schizophrenia, other major psychoses, or neurological disease is established at McLean Hospital.

Dopamine and Chronic Antipsychotic Drug Treatment
MH 28216; $37,191

Bowers, Malcolm B., Jr.
Yale University
New Haven, CT

Central dopaminergic activity is investigated in animals and humans. The effects of a single dose of haloperidol or thioridazine or of chronic administration of fluphenazine or chlorpromazine on dopamine metabolism are compared in several regions of rabbit brain and in plasma and cerebral spinal fluid samples. Chronic and acute studies of chlorpromazine, haloperidol, and thioridazine are made in schizophrenic inpatients. Clinical response is correlated with changes in cyclic adenosine monophosphate, dopamine metabolites, and γ-aminobutyric acid levels.

Clinical Science Research Center in Psychiatry
MH 30929; $540,210

Bowers, Malcolm B., Jr.
Yale University
New Haven, CT

A mental health clinical research center is established for research in the neurobiological bases of psychiatric disorders. Subjects include infants, children, adolescents, and adults. Studies include:

Wexler, Bruce: Regional Neuropsychologic Function and Mental Illness.

VanDyke, Craig: the Psychopharmacological Treatment of Depression in the Elderly.

Redmond, D. Eugene: Adrenergic Antagonists in the Treatment of Appetite Disorders and Neuroendocrine Regulation.

Maas, James: Neurobiologic Bases of Major Psychiatric Disorders; Neurotransmitters and Brain Function, An Approach to Clinical Application.

Swigar, Mary E.: Clinical and Biologic Studies in the Prediction of Antidepressant Drug Response in a General Hospital Setting.

Davies, Robert: The Use of Phenytoin in Syndromes Involving Dyscontrol of Behavior.

Davies, Robert: Prediction of Phenothiazine Response in Neurologically Normal and Abnormal Schizophrenics.

Nelson, J. Craig: Clinical Response to Dosage Adjustment of Imipramine Therapy Using Plasma Concentrations as a Guide.

Lieb, Julian: A Double-Blind Comparison Trial of a Tricyclic Antidepressant (Imipramine) Versus a Monoamine Oxidase Inhibitor (Phenelzine) in the Treatment of the Depressed Phase of Bipolar Affective Disorders in Outpatients Maintained on Lithium Carbonate.

VanDyke, Craig: A Comparison of Perphenazine and Diazepam in the Treatment of Acute Brain Syndrome.

Byck, Robert: Acute Effects of Cocaine in Man.

Giller, Earl: Metabolic Studies in Human Behavior Genetics. In this series of studies, cell culture techniques are used to study the genetic component in schizophrenia, manic-depressive illness, and some other forms of depression.

Cohen, Donald J.: Neurochemical Studies of Psychiatric Disorders of Childhood and Adolescence.

Cohen, Donald J.: Psychobiological and Behavioral Methods for Characterizing Psychiatric Disturbances in Childhood and Adulthood.

Ferholt, Julian: Neuroendocrine and Behavioral Studies of Young Children with Growth and Psychophysiological Disorders.

Genel, Myron: Personality Development in Short Statured Children.

In addition, a series of studies is undertaken to describe in detail the symptomatic, cognitive, perceptual, and biological characteristics of the recovery and recurrence processes in patients with schizophrenia and related psychotic disorder, and to describe in detail the nature of the state of being in remission.

Still another series of studies assesses treatment outcome for ambulatory schizophrenic patients and alcoholics; delineates the correlates of change from the psychotic to the remitted state in schizophrenic patients; develops more refined and reliable methodology in psychiatric diagnosis; investigates the long-term neurological effects of phenothiazine maintenance treatment of the schizophrenic patient compared with maintenance treatment with antidepressants; determines the effects of four distinct psychosocial settings on medication maintenance treatment; and investigates the impact of treatment on outcome.

In another group of studies, the validity of the distinction of schizophrenic from schizoaffective disorder is investigated, and an effort is made to advance the methodology of establishing the validity of categorical diagnostic distinctions in psychiatry.

Training at many levels for various periods of time is part of the research center's activities.

In 1980, core facilities established during the first years of operation continue to perform research relevant to the treatment of severe psychiatric disorders of childhood and adulthood. The core facilities are the Clinical Methodology and Data Processing Unit; the Clinical Neuropsychopharmacology, Mass Spectrometry Facility; the Neuropsychopharmacology Laboratory for the Analysis of Psychotherapeutic Drugs and Metabolites; and the Laboratory of Developmental Neurochemistry. The Clinical Methodology and Data Processing Unit provides consultation and methodological and statistical guidance in the design of clinical projects and in the analysis of data. The Clinical Neuropsychopharmacology Laboratory, Mass Spectrometry Facility, located at the Connecticut Mental Health Center, provides assays of plasma, urine, and cerebral spinal fluid monoamine metabolites using mass spectrometry, gas chromatography, and high performance liquid chromatography. The Neuropsychopharmacology Laboratory for the Analysis of Psychotherapeutic Drugs and Metabolites, located in Yale-New Haven Hospital, is engaged in the assay of tricyclic antidepressants and methylphenidate, and in the development of other assays. The Laboratory of Developmental Neurochemistry (also known as the Child Study Center) measures trace levels of neurotransmitters and their metabolites by high performance liquid chromatography coupled with ultraviolet, fluorimetric, and electrochemical detectors.

Electroencephalogram in Language and Cognitive Process and Dysfunction

MH 00021; $10,492

Brown, Warren S., Jr.
University of California
Los Angeles, CA

The electrophysiological correlates of perception of linguistic meaning are studied as an approach to learning more about the neural basis of language processing and associated cognitive functions. Previous studies have indicated a difference in evoked potentials for the right and left hemispheres of the brain in response to identical words in different contexts as stimuli (as a noun versus as a verb, active versus passive). The goals are to determine the anatomic locus of these differences; define the initial linguistic parameters responsible for the differences (lexical meaning, part of speech, active versus passive); and the effect of brain lesions on the differences. Normal and abnormal language development are studied. A number of pathological conditions in which language and thought disorders are the central features are investigated—e.g., aphasia, dyslexia, and schizophrenia.

Haloperidol and Attentional Learning in Autism
MH 032212; $178,248

Campbell, Magda
New York University Medical Center
New York, NY

The effects of neuroleptic medication on various aspects of the behavior and cognitive performance of autistic children are studied. The therapeutic value of haloperidol on behavioral symptoms, discrimination learning, and selective attention on autism is investigated. Short- and long-term safety of drug therapy using haloperidol is assessed. Subjects are hospitalized, autistic children between 2 and 6 years old.

Children's Psychopharmacology Unit
MH 04665; $124,181

Campbell, Magda
New York University Medical Center
New York, NY

This project involves children, ages 2 to 7 years, diagnosed as having infantile autism according to *DSM–III* (1980) criteria. The main objectives are to assess critically and objectively the effects of haloperidol on behavioral symptoms, on learning, and in a prospective fashion, its effects on the development of neurological neuroleptic-induced movements and growth. Learning is evaluated with the use of an automated data collection system. Blood levels of haloperidol and of prolactin are also assessed and related to behavioral outcome as well as to the development of neurological neuroleptic-induced movements. Prenatal and perinatal complications of pregnancy, electroencephalogram recordings, soft signs, minor congenital abnormalities, and laterality are assessed in addition to behavioral variables. The study is double-blind and placebo controlled. It consists of two phases: a short-term (14 weeks) and a long-term phase (up to 3 years). In the short-term phase, a within groups and a between groups comparison is used. In the long-term phase, subjects are randomly assigned to continuous and intermittent haloperidol maintenance periods of 6 months followed by periods of 4 weeks on placebo.

This project is a major contribution in assessing the short- and long-term safety of haloperidol in autistic children, and its effects on learning and on behavioral symptoms. It also has relevance for other types of populations of children treated with neuroleptics, including those who are mentally retarded. This is a prospective project to study neurological neuroleptic-induced movements in a population who have such a high rate baseline of nondrug-induced abnormal movements.

The use of haloperidol is also explored for treatment of nonpsychotic, severely aggressive, explosive undersocialized children 6 to 12 years of age. In this double-blind study, the effects of haloperidol are compared to those of lithium and placebo. In addition to behavioral assessments, the effects of these drugs on cognition are evaluated.

Parental Mental Illness and Outcome in At-Risk Children
MH 35116; $132,055

Cantwell, Dennis P.
University of California
Los Angeles, CA

This is a 4-year longitudinal study of the effects of parental mental illness on 500 children with communication disorders who were systematically evaluated 4 years earlier at the Community Speech and Hearing Clinic in Encino, California. Half of the children also had a psychiatric disorder at initial evaluation. Almost half live in homes with two parents with psychiatric diagnoses; 15 percent have one parent with a psychiatric diagnosis. Outcome is assessed in three areas: presence and type of psychiatric disorder and symptomatology; presence and type of nonlanguage developmental disorders, such as learning disorders; and speech and language functioning. Children are between the ages of 5 and 19 years at followup.

Hemodialysis in Schizophrenia: An Evaluation
MH 32720; $191,270

Carpenter, William T., Jr.
University of Maryland
Baltimore, MD

The hypothesis that hemodialysis has a therapeutic effect in schizophrenia is investigated. The research utilizes a blind crossover design in which half of the cohort begins with active dialysis and half with sham dialysis. Approximately 33 to 34 patients receive 16 weeks of actual and sham dialysis.

Data Documentation for Clinical Psychopharmacology
MH 33922; $48,568

Cassano, Giovanni B.
Universita degli Studi di Pisa
Pisa, Italy

An international clinical trials documentation system is developed for psychotropic drug assessment, establishing a Center for Clinical Psychopharmacology Data Documentation at Pisa, Italy. European and American clinical trials data are shared using common, standardized, widely acceptable data forms in the system. Several computer systems are merged in this collaboration. A postmarketing assessment system is tested and implemented; additional scales are developed; and dissemination of information is encouraged.

Studies of Schizophrenia Prone Young Adults
MH 31067; $155,977

Chapman, Loren J.
University of Wisconsin
Madison, WI

Scales are developed to identify schizophrenia-prone individuals (individuals at high risk both for brief episodes of psychosis and for schizophrenia). The scales relate to anhedonia (reduced capacity for pleasure), perceptual aberrations, ambivalence, self-esteem, dependency, self-control, and interpersonal adversiveness. Validational criteria of the scales are poor adjustment, and the report of brief episodes resembling schizophrenia, deterioration of adjustment and an increase in certain symptoms over a 2-year period, and poor performance on several measures which are thought to measure defects of schizophrenics and/or the schizophrenia prone. The research involves testing approximately 2,700 college students, and selecting certain subjects for more intensive study.

Impact of Mental Illness on the Family
MH 19649; $19,098

Clausen, John A.
University of California
Berkeley, CA

Data are collected and analyzed relating to the recognition, response, and long-term adaptation to severe psychiatric illness (schizophrenia, manic-depressive psychoses, or severe neurosis) by families of mental patients. Interviews conducted from 1952 to 1960 with the husbands or wives of hospitalized patients provide data on more than 50 families in Washington, DC, and the Maryland suburbs. Two series of interviews in 1971 to 1973 obtained in the Washington area and in the San Francisco Bay area provide supplemental data. Findings of the earlier research are compared with those gathered approximately 20 years later. Long- and short-term followup of patients and their families assesses factors influencing the long-term impact of mental illness and hospitalization. Coping mechanisms of wives and husbands, reintegration of patients into society, and the effectiveness of mental health services to see how much they include other family members are examined. Changes in societal attitude and treatment approaches are studied. The long-term development of offspring is observed.

The Prevention of Tardive Dyskinesia
MH 32675; $174,288

Cole, Jonathan O.
Boston Mental Health Foundation, Inc.
Boston, MA

The causes, prevention possibilities, and treatment of tardive dyskinesia are studied in individuals with early dyskinesia or with severe dyskinesia, and in individuals at risk for developing tardive dyskinesia because of exposure to neuroleptic drugs. Epidemiological studies are made of risk factors related to the presence or absence of dyskinesias after drug treatment and of the incidence of dyskinesias. The progression and classification of dyskinesias are also studied. The effects of lithium on dyskinetic movements are examined in a placebo-controlled study.

Other drugs of possible therapeutic value, including lecithin, clorazepam, and clozapine-like drugs, are examined. Chronic schizophrenic patients who respond well to lithium are also characterized.

Multiorienting Response in Communicational Disorders
MH 031118; $14,952

Condon, William S.
Boston University
Boston, MA

Normal children and children with severe communicational disturbances are compared for differences in orienting responses (head and/or eye movements) to auditory stimulation. The technique for analyzing orienting responses to stimulation entails filming children at 30 frames per second and making a frame by frame analysis to quantify the time sequence and nature of motor activity. The multiple orienting responses in an autistic child seem to indicate that the child is receiving the same sound input multiple times. This supports the hypothesis that there are points where these children exhibit real contact with the world, but in the form of distorted response structures. Subjects are 10 normal children and 10 autistic children between the ages of 7 and 15.

Cingulotomy for Pain and Psychiatric Disorders
MH 32230; $113,160

Corkin, Suzanne H.
Massachusetts Institute of Technology
Cambridge, MA

An assessment is made of the therapeutic outcome, neurological status, and behavioral test performance of patients who have undergone bilateral anterior cingulotomy for the relief of persistent pain or for the alleviation of severe psychiatric symptoms. Patients are interviewed and examined before and after the operation and are compared with patients who do not receive cingulotomies and with normal subjects. The research aims are to specify which types of patients are improved by cingulotomy, and to describe the neurological and behavioral effects of the surgical procedure, whether transient or lasting. Effects are assessed by conducting psychiatric evaluation, neurological examinations, and neuropsychological examinations relating to cognitive, sensory, and perceptual functions. Cingulotomy subjects have severe pain or a diagnosis of schizophrenia, depression, obsessive-compulsive neurosis, anxiety neurosis, or another disorder.

A Pilot Study of Attention in Schizophrenia
MH 34206; $12,789

Cornblatt, Barbara A.
New York State Psychiatric Institute
New York, NY

A pilot study is carried out to establish norms on three attention measures. Three groups are compared: normal subjects, hospitalized schizophrenic patients, and hospitalized depressed patients. The measures are the Continuous Performance Test, the Attention Span Test, and the Information Overload Task.

Multiple Dopamine Receptors and Antipsychotic Drugs
MH 00316; $41,179

Creese, Ian N.
University of California at San Diego
La Jolla, CA

The possibilities of two or more distinct dopamine receptors in the central nervous system are examined in a series of studies. Dopamine binding properties after manipulation of sodium or manganese levels are compared; the binding of dopamine agonists and antagonists are mapped in several areas of rat and calf brain, searching for nonparallel binding sites; differential effects of lesioning on agonist and antagonist binding are examined; and efforts are made to dissociate dopamine binding sites from dopamine sensitive cyclase sites, and supersensitive dopamine receptors from other dopamine receptors.

Genetics of Schizophrenia-Related Deficits
MH 34114; $183,768

Cromwell, Rue L.
University of Rochester
Rochester, NY

A group of schizophrenia-related deficits are measured in extended families with multiple instances of process schizophrenia, extended families with only one known instance of process schizophrenia, and extended families with no psychiatric problems. Segregation patterns are determined for each of the deficits, and where appropriate patterns occur, genetic linkage analysis is performed for gene mapping. Traits studied include reaction time crossover, span of apprehension, platelet monoamine oxidase, serum dopamine β-hydroxylase, and an electroencephalographic measure, average evoked response augmentation/reduction. Interrelationships between the schizophrenia-related traits are also investigated.

Sleep and Its Disorders
MH 05804; $39,486

Dement, William C.
Stanford University
Stanford, CA

Sleep states are electrophysiologically recorded in cats and humans, including schizophrenic and alcoholic patients. Data obtained are correlated with measurements of the metabolism of biogenic amines with an ultimate aim of aiding in the clarification of the mechanisms of psychosis, such as hallucinations and delusions.

In 1980, one study is directed toward providing normative data on normal sleepiness and alertness in older children and adolescents. Another study is concerned with neurochemical and neurophysiological aspects of a strain of narcoleptic dogs. Further research relates to sleep and sleepiness in the elderly, chronobiological mechanisms of sleep/wakefulness, pathological sleepiness, and insomnia.

Hemodialysis for Schizophrenia: A Double-Blind Study
MH 33665; $269,802

Doerr, Hans O.
University of Washington
Seattle, WA

The hypothesis that hemodialysis has a significant therapeutic effect for nonuremic chronic schizophrenic patients is tested. Approximately 24 drug-free outpatients participate in the study, which utilizes a triple-blind protocol with a flexible crossover design, in which patients either begin with regular hemodialysis and crossover to sham dialysis, or begin with sham dialysis and crossover to regular hemodialysis. Therapeutic effects are measured by improvements in social functioning and reductions in the symptoms of schizophrenia. Dialysate and venous samples are collected for future analysis, should a beneficial effect of the treatment be demonstrated.

Monoacylcadaverines in Human Blood
MH 34190; $132,428

Dolezalova, Hana
Stanford Research Institute International
Menlo Park, CA

The levels of the polyamine cadaverine and several of its metabolites are compared in the blood of mental patients, neurological patients, patients hospitalized for other reasons, and in normal subjects at Norwich Hospital in Norwich, Connecticut. The possibility that these compounds are markers for schizophrenia or are involved in the biochemistry of the illness is investigated.

Monoamine Oxidase: Membrane and Human Blood Studies
MH 19734; $102,589

Eiduson, Samuel
University of California
Los Angeles, CA

Different forms of the enzyme monoamine oxidase (MAO), and their regulation of biogenic amines in different brain structures, especially during development of the brain, are studied in human blood platelet samples and animal blood and neural tissue. The biochemical properties of Type-A and Type-B MAO, its physical/chemical properties as revealed by electron spin resonance techniques, its activity in developing brain cells, and its significance and possible aberrant forms in certain neural disorders are examined in this project. The subjects include mongoloids, autistic children, and depressed or schizophrenic adult mental patients, from whom blood samples are taken. Brain tissue and blood from developing and mature chicks, rats, and mice are also studied.

Communication Through Nonverbal Behavior
MH 11976; $106,403

Ekman, Paul
University of California
San Francisco, CA

This investigator is attempting to determine what classes of information are conveyed by nonverbal behavior and how these classes are related to particular body areas, personality types, and culture. He is also interested in the changes in nonverbal behavior of mental patients over the course of hospitalization. Schizophrenic and depressive patients and normal children and adults participate in this research.

As the research progresses over the years, the goal continues to be to study facial expressions and body movements. Emphasis is placed on the development of the

Facial Affect Coding System, a system for recording facial muscle actions which are distinguishable to an observer. The facial and body movements are studied during conversations and interviews using a videotape technique. Efforts are directed toward establishing the reliability, validity, practicality, and application of the analysis and scoring system. How the nonverbal behaviors studied reveal information relevant to emotion and the occurrence of deception is of interest.

Prospective Study of Children of Schizophrenic Parents
MH 19560; $355,868

Erlenmeyer-Kimling, L.
New York State Psychiatric Institute
New York, NY

A longitudinal study of children considered at high risk for the development of schizophrenia because they have one or more schizophrenic parents is performed. Two samples of children, 7 to 12 years of age, are initially assessed through home visits, psychiatric evaluation, psychological tests, laboratory procedures (related to neurological, psychophysiological, cognitive, attentional, and motor factors), and life history data (recorded retrospectively from birth). The children are reassessed approximately 2 and 9 years later.

In 1980, emphasis is placed on measures relating to attentional and information processing deficiencies and on neurophysiological dysfunction. Attention is given to factors that differentiate vulnerable and resistant children within the high-risk groups. Long-term goals of this research are directed toward analyses of biological/environmental interactions, and toward instrumentation of preventive intervention programs based on a more firm understanding of etiological factors and the premorbid state.

Family Therapy for Relapsing Schizophrenics
MH 33138; $115,407

Falloon, Ian R.
University of Southern California
Los Angeles, CA

Two forms of therapy for schizophrenic patients are compared. The first form of treatment is intensive family therapy in combination with an optimal dose of antipsychotic medication. The family therapy aims specifically at reducing high levels of expressed emotion in the family milieu. It includes communication training and problem-solving training designed to strengthen the family's ability to cope with stress. The second form of therapy is individual supportive psychotherapy utilized in combination with medication. Forty families with a schizophrenic member are studied over a 2-year period of community care. The project is specifically focused on decreasing the probability of relapse and chronicity in schizophrenic patients.

Neuropsychology of Attention in Infantile Autism
MH 00250; $39,111

Fein, Deborah A.
Boston University
Boston, MA

Behavioral, autonomic, and electrophysiological measures are used to study the characteristics of attentional functioning in autistic children. The following theories are tested with a series of experimental paradigms: variability, failure to associate, inflexible arousal, and faulty switching. Orienting response, habituation, spontaneous recovery and rehabituation, dishabituation, distraction, generalization of habituation, consistency of responding to a particular stimulus, conditionability, response to competing stimuli, interaction between two stimuli, exploratory behavior, and stereotypes are measured.

Schizophrenic Offspring From Birth to Adulthood
MH 31653; $57,136

Fish, Barbara
University of California
Los Angeles, CA

The adult outcomes and life histories of 24 offspring of schizophrenic and nonpsychotic mothers, who have been studied since their births in 1952-1953 and 1959-1960, are evaluated. The research is designed to test the hypothesis that neurointegrative disorders in infancy predict vulnerability to later schizophrenia, to determine the influence of the rearing family and other life experiences, to obtain standardized evaluations of the young adult subjects and their rearing families, and to make the data compatible with other high-risk research samples. The research is especially concerned with a neurointegrative disorder referred to as pan-developmental retardation, a transient dysregulation of motor, visual/motor, and physical development noted between birth and 2 years.

Dreams, Language, and Cognition
MH 32063; $78,030

Foulkes, David
Emory University
Atlanta, GA

A new method of dream analysis called the Scoring System for Latent Structure is studied. The method is based on Freudian theory concerned with the derivation of the manifest dream from a set of underlying dream thoughts. One goal of the research is to develop and refine the model. Another is to make the psychoanalytic dream model consistent with current explanatory models in linguistics, cognitive psychology, psycholinguistics, and neuropsychology. The Scoring System for Latent Structure is applied to dreams, associations, and waking thought specimens from normal adults and several specialized samples including congenitally blind and schizophrenic individuals, in order to address issues relating to cognition in different psychophysiologically assessed states, waking sources of dream content, structural and semantic regularities in dreams, the forgetting of dreams, and thought defects in schizophrenia.

Hyperserotonemia in Autistic and Retarded Children
MH 27399; $116,592

Freedman, Daniel X.
University of Chicago
Chicago, IL

Monoamine metabolism is studied in children and young adults who have high blood levels of serotonin (hyperserotonemia) and frequently suffer from mental retardation or autism. One aim of the research is to identify 10 to 12 males, 12 to 28 years old, with these disabilities. Another goal is to determine where in the blood (plasma, platelets, red blood cells) the elevated serotonin (5-HT) levels are distributed. The biochemical and physiological mechanisms accountable for this are examined. Blood and urine studies in animals with central nervous system (CNS) lesions provide a model suitable for further investigation of disorders in monoamine metabolism originating from central injury. The interrelationships of 5-HT, tryptophan, and pyrrolase occurring in the blood and the liver and consequences of blocking them are studied.

Beginning in 1979, the research is extended to include subjects with Huntington's chorea and schizophrenia.

Behavior Observation Scale for Autism
MH 29248; $80,704

Freeman, B.J.
University of California
Los Angeles, CA

The objectives of this research are: to develop an objective Behavior Observation Scale (BOS) which will differentiate autistic from normal and mentally retarded children (30–60 months of age); to differentiate subgroups of autistic children along various symptom axes; to establish a quantitative continuum of severity within each symptom subgroup; to provide an objective means of describing children who serve as subjects in neurophysiological and neurobiochemical research; and to periodically reevaluate autistic children and thus track the natural course of the disease. Subjects are normal, autistic, and retarded children who are observed in a structured setting. Their behaviors are counted on the BOS. Data obtained on the BOS are subjected to a discriminant analysis which differentiates among groups of children, divides children according to symptom subclusters, and provides a quantitative continuum of severity in each subcluster. These data are cross-correlated with data obtained from developmental histories; psychiatric interviews; and clinical, psychometric, and language evaluations.

Biological Studies of Psychotic Disorders
MH 08618; $327,365

Friedhoff, Arnold J.
New York University
New York, NY

The relationship of metabolic processes, particularly those involving neurotransmitters, to psychotic disorders is investigated in a series of clinical and laboratory studies.

The metabolic roles and significance of dimethoxyphenylethylamine (DMPEA), dopamine, and monoamine oxidase (MAO) are investigated in studies of schizophrenia. Examination is made of the effects of neuroleptics or of genetic determinants on MAO or other enzyme and metabolite levels; dopamine release, turnover, uptake and interactions with other neurotransmitter systems; and of DMPEA metabolism. Electrophysiological and metabolic correlates of administration of neurotransmitters, major tranquilizers, or alcohol are also examined in patients and in control subjects.

The mechanisms of action of hallucinogens, including mescaline, tetrahydrocannabinol, bufotenin, DMPEA, and LSD are examined in relation to acetylcholine metabolism and to the possible production of endogenous hallucinogens. Transmethylation reactions are also examined in relation to psychiatric symptomatology and hallucinatory phenomena.

Animal models of depression and amphetamine psychosis are studied. Clinical and laboratory studies of the relation of tardive dyskinesia to dopamine receptor sensitivity are made, and the therapeutic, metabolic, and behavior effects of lithium are studied in humans and animals. The relation of therapeutic radiation, heart surgery, or childhood lead-poisoning to psychiatric disease is also examined.

Standardized quantifiable methods are developed for recording childhood behavioral maladaption, and for collection of investigative and epidemiological data. Tremor is measured in patients treated with antipsychotic drugs. Studies are also made with patients with a diagnosis of schizophrenia or alcoholism, of verbal and vocal parameters, correlations of reaction latency to intoxication, and the relation of suggestion, arousal and stimuli to auditory hallucinations.

Immunological methods for measuring altered creatinine kinase isoenzyme levels in the blood of schizophrenics are tested.

In 1981, this project focuses on the mechanisms underlying receptor sensitivity modification and ultimately its role as a therapeutic regimen. Measurements are made of the responses of neuronal receptor cells in animals to antagonist, agonist, and chronic pharmacological treatments. Brain enzyme analysis and biochemistry studies further explore the prenatal exposure influence on postnatal receptor development. Pregnant rodents are exposed to neuroleptics and to stress in tests for γ-aminobutyric acid (GABA) receptor density and diazepam binding. Psychiatric patients are being used to determine if platelet monoamine oxidase (MAO) can be used as an experimental model for brain MAO.

Chemical Factors in Abnormal Behavior
MH 14024; $19,520

Friedhoff, Arnold J.
New York University
New York, NY

Drug-induced and other psychoses are examined in a series of studies. The effect of mescaline on adenosine triphosphate catalyzed reuptake of dopamine by nerve cell membrane preparations is investigated. The interaction of dopaminergic and cholinergic compound in the production of psychosis, and the mechanism of action of amphetamine-produced psychosis are examined. The possible role of enzyme induction in the pathogenesis of alcoholism and drug addiction is studied. The effects of antipsychotic drugs on dopamine receptors are investigated in rat brain. The influence of antipsychotic medication and withdrawal on platelet monoamine oxidase activity is examined in schizophrenics. Dimethylphenylethylamine (DMPEA) excretion in schizophrenics and normals is correlated with the activities of two forms of the enzyme catechol-O-methyltransferase (COMT). Both forms of COMT are studied for their involvement in the production of toxins in schizophrenia. Clinical studies of modifications of dopamine receptor sensitivity in patients with tardive dyskinesia, Tourette's Syndrome, and Huntington's chorea are extended to animal studies involving the affinity of receptors for neurotransmitters, as well as adenylate cyclase activity, after induction of receptor supersensitivity with drugs. Brain peptides which bind to opiate receptors are also investigated.

In 1981, the study is continued on the role of dopamine and other neurotransmitters, and the involvement of regulator mechanisms in mediating normal and psychotic states. The mechanisms of receptor modification by antagonists are examined, especially the relationship of dose regulation and duration of treatment with a dopamine-blocking agent to changes in receptor density. The consequences of receptor sensitivity modification on brain biochemistry (including calmodulin's influence on adenylate cyclase) and the behavioral implication of these changes are investigated in animals. Use of a combination of L-dopa with an antipsychotic is explored in the search for dopaminergic antagonists which would prevent development of the tardive symptom in tardive dyskinesia. Studies of the prenatal factors affecting neurotransmitters in postnatal brain development are undertaken. Prenatal effects of the neuroleptics on the development of γ-aminobutyric acid (GABA) receptors in rats are investigated with haloperidol, chlorpromazine, or sulpiride. The influence of haloperidol administration on cholinergic and muscarinic receptors and on choline acetyltransferase activity is also followed. The norepinephrine and GABA receptors are examined in relation to stress and anxiety, and the benzodiazepine receptors in relation to GABA. Effects of chronic neuroleptic drug treatment on central nervous system monoamine oxidase (MAO) content are investigated, and a comparison of MAO in platelets is made.

Children Vulnerable to Psychopathology
MH 14914; $32,400

Garmezy, Norman
University of Minnesota
Minneapolis, MN

The project studies the earliest precursor signs of maladjustment in children who are at high risk for later psychopathology, particularly schizophrenia. The strategy of the studies involves the selection of those children in a community whose risk ratio is high because of genetic loading (for instance, biological parents who are psychotic), family disorganization, or presumed pathogenic influences that exist in highly disadvantaged areas of the city. Three basic models for the etiology of mental disorder are examined: first, transmission; second, pathology of the near environment (the family); and third, the pathogenic influence of poor sociocultural environments.

Biology of Schizophrenic Subtypes
MH 32666; $144,730

Garver, David L.
University of Cincinnati
Cincinnati, OH

The hypothesis that a subgroup of schizophrenic patients exists showing evidence of dopamine receptor supersensitivity, increased platelet adenylate cyclase activity, and normal platelet monoamine oxidase activity is tested. It is further hypothesized that this subgroup of patients responds favorably to physostigmine challenge and treatment with lithium. Extensive biological and psychological data are collected for approximately 80 patients admitted with a diagnosis of schizophrenia or schizoaffective disorder. Family history is collected for first degree relatives of these index cases.

Oral Lecithin for the Treatment of Tardive Dyskinesia
MH 32993; $41,231

Gelenberg, Alan J.
Massachusetts General Hospital
Boston, MA

The efficacy of a lecithin dietary supplement in treating tardive dyskinesia is investigated in double-blind crossover studies in psychiatric patients with tardive dyskinesia—mainly schizophrenic patients—who have received neuroleptic drugs.

Fibroblast Monoamine Metabolism and Psychoses
MH 31256; $15,209

Giller, Earl L., Jr.
Yale University
New Haven, CT

This pilot project is concerned with establishing skin fibroblast lines from patients with reliably diagnosed psychiatric disorders and examining monoamine metabolism in these cell lines. The properties of monoamine oxidase and catechol-*O*-methyltransferase and other enzymes and proteins of monoamine metabolism are studied in schizophrenic and manic-depressive patients.

Role of Biogenic Amines in the Central Nervous System
MH 02717; $121,168

Goldstein, Menek
New York University
New York, NY

This project examines enzymatic regulation of biosynthesis and metabolism of biogenic amines. The effects of certain drugs, including amphetamine and ethanol, on biogenic amine production and use are studied. Radioactive tracers are used to follow catecholamine synthesis and degradation. Subjects are humans, monkeys, cats, and rats; human subjects are psychiatric inpatients. Both activity and diet are carefully controlled during the study. Immunocytochemical and radioimmunoassays are developed for enzymes involved in catecholamine synthesis, and used for location of catecholamine systems in primate and human postmortem brain tissue. Molecular mechanisms of neuroleptic drugs and apomorphine are investigated in these systems. Tyrosine hydroxylase activity is used to screen antipsychotic drugs. Investigations are made on the influence of cold stress, hypertension, and hormones on the function of epinephrine systems. Other neurotransmitters, including acetylcholine and γ-aminobutyric acid, are also examined.

In 1981, this project continues to investigate pathways, mechanisms of action, and physiological significance of the biogenic amines. The following studies are included: examination of the mechanisms activating tyrosine hydroxylase's activity using cyclic adenosine monophosphate-dependent protein kinase; study of the effects of chronic administration of neuroleptics and norepinephrine and epinephrine turnover; investigation of the influence of epinephrine neurons on norepinephrine and dopamine neurons in regulation of pituitary hormones; and measurement of specific dopamine receptors to determine if they function coordinately or independently. The use of thermostability is explored as a tool to characterize multiple dopaminergic receptors, distinguishing those with high affinity for agonists from those with a high affinity of antagonists. Another investigation pursues the locations and modes of activation of other monoaminergic-synthesizing enzymes, starting with purification of antibodies to trytophan hydroxylase and histidine decarboxylase.

Amine Metabolism and Its Relation to Mental Disease
MH 14918; $39,204

Goldstein, Menek
New York University
New York, NY

The investigator is studying the role of biogenic amines in the central nervous system and in various mental and neurological disorders. The following areas are being investigated: enzymatic studies on the biosynthesis of biogenic amines in patients with psychiatric and neurological disorders; the cellular localization of enzymes involved in the biosynthesis and metabolism of biogenic amines; the control mechanisms of catecholamine synthesis in neuroblastoma tumor tissues; and the interactions between monoaminergic-containing neurons in the central nervous system. Mice and monkeys are the subjects.

In a subsequent period, studies of the interactions between various neurotransmitter systems at the morphological and molecular level continue. Various monoaminergic neuronal systems are mapped in the murine and primate central nervous systems. In another study, the effects of neuroleptics on the dopamine system are investigated. A test is developed for predicting antipsychotic activity of drugs and for measuring plasma neuroleptic levels in schizophrenic patients. In yet another study, the role of monoamines in extrapyramidal dysfunctions such as tremor and abnormal involuntary movements is investigated. Monkeys with surgically induced tremor and hypokinesia serve as models for studying the effects of centrally acting drugs on these dysfunctions.

In 1980, the catecholamine function is characterized in several experiments aimed at discovering the biosynthesis mechanism. The following problems are examined: role of cyclic adenosine 3', 5-monophosphate (cAMP) and presynaptic dopamine receptors in the regulation of tyrosine hydroxylase; repeat administration of dopamine agonists and antagonists on the dopamine neuronal systems; multiple dopamine receptors; and epinephrine neurons in the central nervous system.

Coping Behavior in Schizophrenia
MH 08744; $152,710

Goldstein, Michael J.
University of California
Los Angeles, CA

A longitudinal study is made of intrafamilial antecedents to schizophrenia. Focus is on troubled adolescents, their family interaction, their communication styles, and their coping patterns as factors in the development of adult psychopathology. Sample population consists of 65 index adolescents (average age 16 years), comparison siblings, and parents. Four groups are differentiated on the basis of symptoms: aggressive, antisocial; active family conflict; passive negative; and withdrawn, socially isolated. Three lines of experimental investigation are followed. The first is an examination of parent-child interaction in families of nonpsychotic, disturbed children; patterns of behavioral response to stress are examined to identify components which may contribute to the shaping of coping patterns characteristic of adult schizophrenics. The second is an assessment of factors in intrafamilial relationships which may differentiate groups of disturbed adolescents who vary in types of presenting problems. The third is an attempt to relate the type of familial interaction of specific patterns of coping behavior shown by disturbed adolescents in a variety of experimental tasks.

In 1975, in addition to the continuing longitudinal study, research is performed on family interaction patterns of nonhospitalized, disturbed adolescents and hospitalized psychotic adolescents; adolescent behavioral and intrafamilial transactions which may be precursors of early adult schizophrenia; the impact of therapeutic intervention on families of high-risk adolescents; and development of specific therapeutic intervention procedures tailored to fit the distortions in intrafamilial interactions significant for the development of schizophrenia.

Beginning in 1978, 5-year followup data for the basic longitudinal study are analyzed. In addition, family data from 10 inpatients with anorexia nervosa are compared with family data for inpatients with schizophrenia or borderline psychosis.

In 1981, the longitudinal study is extended to include a 10- to 12-year followup. Other studies also continue. In addition, another major group of studies concerned with communication deviance, affective style, and expressed emotion in the parents of schizophrenic patients is initiated. The studies are performed in collaboration with three different institutions: Camarillo State Hospital, Ventura, California; Western Psychiatric Institute, Pittsburgh, Pennsylvania; and the University of Southern California, Los Angeles, California.

Metabolite Profiling of Antipsychotic Drugs
MH 32525; $71,887

Green, Donald E.
University of San Francisco
San Francisco, CA

A profile of chlorpromazine metabolites is developed for human plasma and urine; this profile is then correlated with treatment response to chlorpromazine in hospitalized schizophrenic patients at the Veterans Administration Hospital in Palo Alto.

Functional Brain Asymmetry in Psychosis
MH 30456; $98,614

Gur, Raquel E.
University of Pennsylvania
Philadelphia, PA

The nature of functional brain asymmetry is investigated in nonparanoid and paranoid schizophrenics. The first study focuses on asymmetry as manifested by dichotic presentation of verbal material to the left hemisphere and musical material to the right hemisphere. In the second study, verbal and spatial stimuli are presented tachistoscopically and subject performance, while solving the problems in each hemisphere, is examined. The third study assesses the relation between schizophrenia and hemisphericity (the tendency to rely primarily on one, rather than another cerebral hemisphere), and their relation to problem solving by measuring conjugate lateral eye movements as an index of hemispheric activation. The fourth study assesses subject performance on a test which requires visual information processing in a simultaneous (presumably left hemisphere) and successive (presumably right hemisphere) fashion.

Later studies beginning in 1978 are designed to test hypotheses about cerebral dysfunction and psychopathology. Hemispheric laterality is investigated through numerous experiments in which data are gathered from inpatients who are left-handed or right-handed with diagnoses of schizophrenia, affective disorders, or brain damage. A final study is concerned with the development of laterality in newborn infants. Infants whose mothers manifest psychotic symptoms are examined between 6 hours and 29 hours old, between 30 and 43 hours old, and between 54 and 77 hours of age. Laterality measures of infants' mothers and fathers and indicators of natal brain trauma are intercorrelated.

Chronic Mental Patients in the Community for 20 Years
MH 29575; $129,965

Harding, Courtenay M.
University of Vermont
Burlington, VT

A followup study of 253 former mental patients, originally selected for chronic disability, who were rehabilitated and released from Vermont State Hospital in the 1950's, is performed. Most of the patients had a diagnosis of schizophrenia, but others had a diagnosis of primary affective disorder, or other psychiatric illness. The study has as its aim a determination of the life style of the former mental patients, including living arrangements, relationships with others, work history, extent of disability, type of community support systems required, and availability and utilization of these systems. The results should contribute to a more detailed and precise delineation of the community care concept for chronic patients, the impact of the illness on family life, the types of employers who hire former mental patients, the rate of recidivity, and the prognostic predictors correlated with outcome variables. Information is obtained through direct interviews with patients, a questionnaire, the Mental Status

Examination Record, and old hospital records. The results of a 5-year followup of the patient group studied were published in a book entitled *The Vermont Story*.

Parents as Speech Teachers for Autistic Children
MH 29897; $63,678

Harris, Sandra L.
Rutgers University
New Brunswick, NJ

The feasibility and effectiveness of teaching general principles of behavior modification to parents of nonverbal autistic children, 2½ to 4 years old, are examined. Techniques for training parents to teach speech to their own autistic children are studied. The measures of behavioral change focus upon periodic home and laboratory observation of speech and behavior. Home versus laboratory-based training, group versus individual family training, and focused training in speech skills, plus training in broad behavior modification skills versus speech training only are evaluated. Systematic followup at 3, 6, and 12 months occurs in all studies so that portions of some studies are in progress while new studies are initiated.

Schizophrenic Cognition: A Longitudinal Study
MH 26341; $150,567

Harrow, Martin
Michael Reese Hospital and Medical Center
Chicago, IL

A systematic investigation of the nature and longitudinal course of schizophrenic thinking is being conducted. Schizophrenic and nonschizophrenic patients are evaluated for cognitive functioning during the acute stage of their illness and during partial recovery. They are then followed up during the posthospitalization period in terms of disordered thinking, symptom status, rehospitalization, and social and work adjustment. One aim of the research is to determine if there are fundamental thought disorders which are always present in schizophrenics, or if specific groups of schizophrenics, such as reactive schizophrenics, exhibit distinguishable types of pathology. Another objective is to discover whether traces of thought disorders persist after the patient has recovered from his illness. The prognostic value of different types of thought disturbances is analyzed, and the long-range significance of differing cognitive styles—modes of organizing or classifying perceptual stimuli—is examined. The wide array of tests used to assess cognitive functioning includes the Rorschach and the Goldstein Object Sorting Test.

Environmental/Personal Treatment
MH 30750; $286,807

Hogarty, Gerard E.
University of Pittsburgh
Pittsburgh, PA

A study is made of the influence of family living situation, treatment type, and individual patient characteristics on the posthospital course of individuals with schizophrenic disorders. Interactions are examined between drug treatment, social skills treatment, family environment, and the patient's own residual psychopathology. Performance site is Western Psychiatric Institute and Clinic.

Cell Membrane Activity in Functional Psychoses
MH 26494; $64,125

Hokin, Mabel R.
University of Wisconsin
Madison, WI

Erythrocyte electrolyte transport mechanisms in psychiatric patients suffering from depressive and schizoaffective disorders are examined in this project. A longitudinal study is conducted of individual fluctuations in sodium pump activity, in order to identify any differences which may be specific for bipolar affective disorder. Other phases of the research examine the characteristics of the erythrocyte membrane sodium- and potassium-dependent adenosine triphosphatase (ATPase) in bipolar affective disorder, and attempt to determine whether genetic variance is involved in the condition. Other experiments study the effects of chronic administration of lithium salts on levels of sodium- and potassium-dependent ATPase in the rat and mouse brain, and inbred strains of mice are screened for possible animal model systems. Phospholipid levels and phospholipid metabolism in erythrocyte membranes from subjects with various functional psychoses are also studied. The metabolism of phosphatidic acid and polyphosphoinositides in erythrocyte membranes in different functional psychoses are examined. Parameters of sodium/potassium pump activity are correlated with clinical response in lithium-treated, bipolar or unipolar depressives and in patients with schizophrenia, schizoaffective disorders, and other psychiatric disorders.

Improved Clinical Screening of Phrenotropic Drugs
MH 03030; $111,951

Hollister, Leo E.
Stanford University
Stanford, CA

A broad-based series of studies in clinical psychopharmacology is planned, which includes screening of antipsychotic, antidepressant and antianxiety drugs, testing the therapeutic applications of marijuana and its derivatives, and employing drugs as tools for understanding the chemical nature of psychiatric disorders. The emphasis is on exploratory clinical trials of new approaches to treatment. Antipsychotic drugs not closely related chemically or pharmacologically to current drugs, or showing special types of actions are chosen for study. A clinical trial of thyrotropin-releasing hormone is undertaken in depression, and the effects of the pituitary hormone melatonin on sleep and psychiatric disorders are studied. Very potent sedatives are used to separate sedative from antianxiety effects. Marijuana is tested initially in depressions and in migraine. The clinical pharmacology of levodopa in schizophrenia is explored, to attempt to verify observations that it exacerbates the disorder. The clinical pharmacology of apomorphine is studied for the same purpose. Cholinergic agonists are used in investigations of cholinergic mechanisms in Huntington's chorea, tardive dyskinesia, manic-depressive illness, and schizophrenia.

In 1981, a series of clinical experiments include the following investigations: cholinergic mechanisms involved in the additive effects of choline chloride and lithium administered to patients with bipolar affective disorders; plasma level measurements of patients receiving haloperidol and thiothixene; factors influencing the measurement of urinary excretion of methoxyhydroxyphenylglycol (MHPG); development of a human model for antianxiety drugs using yohimbine and diazepam; levodopa's ability to block dopamine receptors; and an evaluation of patient abuse of diazepam and nordiazepam.

Analysis of Drugs and Psychoactive Phenolic Amines
MH 12007; $61,828

Holmstedt, Bo R.
Karolinska Institute
Stockholm, Sweden

A series of psychoactive drugs are analyzed and examined in animals and in humans. Biogenic phenolic amines, which are present in intoxicating snuff used among South American Indian tribes, are isolated and characterized, using gas chromatography and mass spectrometry. Modern analytical techniques are used to identify drugs and metabolites in cerebrospinal fluid. Serotonin and catecholamine metabolites are examined in patients with depression and other conditions. Chlorpromazine and tetrahydrocannabinol (THC) levels are examined in body fluids. Chemical studies are made of a large number of plants of ethnobotanical and hallucinogenic interest. Effects of drugs on acetylcholine metabolism, drug kinetics, and tetrahydrocannabinol pharmacodynamics are investigated. The endogenous formation of hallucinogenic indoles is investigated in central nervous tissue of animals and in cerebral spinal fluid of human clinical populations, including alcoholic, schizophrenic, and depressed populations.

Psychomotility and Cognitive Style in the Schizophrenias
MH 31340; $89,425

Holzman, Philip S.
Harvard University
Cambridge, MA

The investigator is studying impaired psychomotility across the range of schizoid disorders, from the most to the least severe types of the disease. He is also studying the characteristic perceptual reasoning patterns (cognitive style) of schizophrenics. Acute and chronic schizophrenics, depressed patients, noninstitutionalized schizoids, family members of hospitalized psychotics, and normal individuals participate in this study. Beginning in 1976, three interrelated studies are undertaken: exploration of the eye-tracking dysfunction as a genetic marker; effects of various drugs (Valium, Thorazine or Seconal) on eye-tracking performance in humans, and effects of chlorpromazine, amphetamines, and various psychotomimetic substances with unanesthetized monkeys; and a longitudinal followup of patients with eye-tracking dysfunctions.

Later studies in 1978 continue to investigate the areas of eye-tracking, thought disorder, and cognitive style. The significance of dysfunctions of smooth pursuit eye movements is explored in two twin studies. Two samples, one in the United States and one in Norway, of monozygotic and dizygotic twins discordant for schizophrenia, are compared. The effects of psychotropic medication on the patterning of cognitive controls in patients with a diagnosis of schizophrenia and normal individuals are compared. Studies are made of the response to different doses of haloperidol of schizophrenic patients with thought disorders.

Electrodermal Activity of Children at Genetic Risk
MH 30682; $42,443

Janes, Cynthia L.
Washington University
University City, MO

A prospective, longitudinal investigation of the electrodermal activity of children at risk for psychopathology by virtue of parental psychiatric illness is performed. Electrodermal measures include shape of the skin potential response, recovery rate of the skin conductance response, bilateral differences in electrodermal activity, and other measures. Data are compared with data collected previously on many of the same children 10 years ago so that important developmental trends can be determined. Data are also compared with concurrent measures of social and psychological functioning, evaluated in a larger project (R01 MH024819). Predictions are made about vulnerability to future pathology, as well as resistance to maladjustment. The experimental subjects are children—age range 7 to 23 years—in families in which one parent has been hospitalized for schizophrenia, manic depressive psychosis, or a physical illness. The control group consists of children of psychiatrically normal parents.

Psychopharmacological Study of Psychiatric Disorders
MH 30914; $307,443

Janowsky, David S.
University of California
La Jolla, CA

A Mental Health Clinical Research Center is established to serve as a nucleus of psychiatric research. The emphasis of this research is on the use of psychopharmacologic agents as tools for exploration of psychological, psychophysiological, and neurochemical aspects of affective disorders. Individual research projects are conducted within the Center, some on clinical wards and some with animal subjects. Project titles and investigators include:

Schlapfer, W.: Modulation of Cholinergic Synaptic Transmission in the Abdominal Ganglion.

Knapp, Suzanne: Effects of Divalent Cations on Biogenic Amine Synthesis: Interactions with Lithium.

Pavlinac, Dennis: Psychotropic Effects of Magnesium in Affective Illness.

Kripke, Daniel: Circadian Rhythms in Manic-Depressive Patients.

Segal, David: Behavioral Pharmacology of Lithium.

Huey, Leighton: Psychostimulant Antagonism by Lithium Carbonate.

Janowsky, David: Interactions Between Lithium Carbonate and Cholinesterase Inhibitor.

Janowsky, David: Effects of Intravenous Methylphenidate on Serum Prolactin and Growth Hormone.

Mandell, Arnold: Lithium Stabilization of Serotonergic Biosynthesis Against Effects of the Euphorigens Cocaine, Amphetamine, and Alcohol.

Judd, Lewis: Studies to Identify Psychological and Behavioral Processes Which Accompany or Mediate Therapeutic Changes Induced by Psychotropic Medications.

Huey, Leighton: Biochemical Correlates of Affective Disorders.

Bullard, Wilson: Cerebral Spinal Fluid Biopterin as a Potential Index of Catecholaminergic Status.

Braff, David: Psychophysiological Measures of Information Processing Across Clinical and Drug States.

Hubbard, Bruce: Average Cortical Evoked Response as a Dependent Variable: Its Potential Usefulness in Predicting Drug Response.

Geyer, Mark: Animal Behavioral Models in Relation to Drug Effects and Aminergic Behavioral Mechanisms.

Ferguson, James: Body Image in Depression.

Janowsky, David: The Effects of Psychotropic Drugs and Clinical State on Interpersonal Interactions.

Squire, Larry: The Mechanisms of Memory and Memory Dysfunction.

In 1981, the program in clinical psychopharmacology is continued. Project titles and investigators include:

Janowsky, David: The Role of Acetylcholine in Affective Disorders.

Judd, Lewis L.: Exploration of the Role of Endorphins in the Regulation of Affective and Cognitive Phenomena.

Kripke, Daniel: The Relationship of Time Functions to Psychopathology and Psychotropic Drug Effects.

Pavlinac, Dennis: The Role of Calcium and Magnesium in the Regulation of Affect.

Janowsky, David S.; Effects of Aspects of Cognitive and Psychiatric Disorders.

Judd, Lewis L.: Psychomotor and Cognitive Effects of Psychotropic Drugs in Normal and Psychiatric Patients.

Squire, Larry: Effects of Psychoactive Drugs and Psychopathological Disorders on Memory.

Janowsky, David S.; Effects of Mood State and Psychoactive Drugs on Interpersonal Perceptions and Interactions.

Braff, David, and Geyer, Mark: Early Information Processing Deficit in Schizophrenia and Other States.

Braff, David, and Geyer, Mark: Effects of Drugs and Diagnosis on Startle Reflexes and Blink Responses.

Grant, Igor: Neuroleptic Treatment and the Remission of Schizophrenia.

Schucter, S.: Widowhood: A Study of Bereavement.

Storms, Lowell: Utilization of Clinical Psychologic Testing to Assess Psychopharmacologic Effects.

Collaborative Studies: Interface Between Alcoholism and Other Major Psychiatric Disorders.

Griffiths, John, and Hornbeck, Cecil: Development of a Pharmacokinetic Laboratory.

Ehlers, Cindy: Assays of Psychobiologic Products in Clinical Psychiatric Research.

Huey, Leighton: Cardiotoxicity and Side Effects of Psychotropic Drugs.

Creese, Ian: Investigation of Neurotransmitter Receptors.

Groves, Philip M.: Psychopharmacologic Studies of Synaptic and Neuronal Functioning.

Segal, David: Psychopharmacologic Behavioral/Biochemical Interaction Studies.

Barondes, Samuel: Studies of Neuronal Plasticity and Cellular Recognition.

Mandell, Arnold J., and Russo, Patric V.. Consistencies in the Spectral and Exponential Properties of Variance in Cross-Disciplinary Data: Psychophysiological Syndromes and Psychotropic Drug Treatments.

Low Dose Neuroleptics in Outpatient Schizophrenics
MH 31776; $87,309

Kane, John M.
Long Island Jewish-Hillside Medical Center
New Hyde Park, NY

The efficacies of minimal or standard dose levels of fluphenazine decanoate in long-term treatment of schizophrenic outpatients are compared. Factors such as symptoms of schizophrenia, side effects from the drug, rates of relapse, amount of rejection of medical regime, restabilization, social adjustment, life stress, and perceived burden on the patient's family are assessed for the two dose levels.

The Course of Schizophrenia Among Mexican Americans
MH 33502; $35,869

Karno, Marvin
University of California
Los Angeles, CA

Pilot data are collected for a longitudinal study of Mexican-American schizophrenic patients in the Los Angeles area. The project focuses on expressed emotion in family members as a determinant of outcome in Mexican-American patients as compared to Anglo-American patients. Expressed emotion is measured by the Camberwell Family Interview.

Collaborative Biological Research in Schizophrenia
MH 31154; $525,947

Kety, Seymour S.
McLean Hospital
Belmont, MA

A multidisciplinary research program brings together new developments, techniques, and concepts from fundamental disciplines to bear on the problems of schizophrenia and other major psychoses. The program consists of the following seven laboratories or sections:

Naute, Walle: Neuroanatomy Section. Light microscopic studies are conducted to determine the position of the monoamine neuron systems within the general organization of the central nervous system. Mesencephalic dopamine cell groups are studied as well as the serotonin nuclei of the mesencephalic raphe and central gray substance. Connections of the substantia nigra are examined, in addition to striatal nigral connections.

Walton, Kenneth: Cell Biology Section. Brain cell aggregate preparations are utilized as a model of the developing brain. Sensitivity changes that can be induced in receptor adenylate cyclase systems of the cultured aggregates are examined. Protein phosphorylation is studied in relation to synaptic function.

Kety, Seymour: Genetics Section. The activities of the genetics laboratory center primarily around a Danish sample of adopted individuals with schizophrenic parents. The major aim is to delineate some of the environmental factors which contribute to the development of schizophrenia. Three classes of environmental factors have been indicated: postnatal cerebral injury, season of birth, and sociofamilial factors such as limited maternal survival. HL-A linkage was studied in 1977.

Baldessarini, Ross: Neuropharmacology Section. Studies relate primarily to central nervous system serotonin neurons and behavior, and the use of ligand-binding methods to measure blood and brain levels of neuroleptic drugs in animals. In 1977, research areas included: neurotransmitter release; receptor actions; the relation of cyclic adenosine monophosphate to postsynaptic sensitivity; the effects of antipsychotic drugs on brain protein and ribonucleic acid metabolism; effects of apomorphine or amphetamine on stereotyped behavior in animals; stabilizing effects of neuroleptic drugs on synaptic membranes; transmethylation of psychotomimetic amines; and alterations in monoamine oxidase in schizophrenics.

Holzman, Philip: Psychology Section. Research relates to horizontal pursuit eye movement dysfunctions, thought and language disorders, and attention dysfunctions in schizophrenia.

Lipinski, Joseph: Clinical Investigation Section. This section is performing research on the diagnosis of schizophrenic and other psychotic disorders; the effects of the intravenously administered naloxone on schizophrenic and manic psychoses; receptor antibodies in schizophrenia; and the use of saliva lithium determinations in lithium therapy. Research on the development and clinical application of a binding competitive assay for neuroleptics is also carried out. In 1977, the effects of gluten were considered.

Kety, Seymour: Administration and Core Support Section. This section provides administration and support for the entire program.

Mental Health Clinical Research Center: New York State Psychiatric Institute MH 30906; $524,225

Klein, Donald F.
New York State Psychiatric Institute
New York, NY

A Mental Health Clinical Research Center is established. Major projects include:

Endicott, Jean: Biometric Behavioral and Diagnostic Assessment. A core facility provides research training, consultative, and developmental research activities that improve behavioral and diagnostic assessment of subjects, in order to increase the powers and generalizability of research findings and comparability of research data.

Ross, Donald C.: Computer Facility. A data processing staff serves the entire New York State Psychiatric Institute. Statistical consultation, education, and analysis are provided. This core facility, as well as the diagnostic assessment facility, is intended to allow for the development of interdisciplinary projects in the areas of schizophrenia, affective disorders, and childhood disorders research.

Sutton, Samuel: Evoked Potential Facility. Research in the developmental stage relates to hypothesized lateralized disorders of the cerebral hemispheres in schizophrenic and psychotic depressive patients, evoked potential measures of selective attention in schizophrenia, and evoked potential correlates of noxious or painful stimuli. The evoked potential recorded when a stimulus is not known in advance is also studied.

Bruder, G.: Audition Facility. Preliminary research is concerned with speech and nonspeech measures of central auditory system functioning. Auditory test performances of poor premorbid schizophrenic patients, good premorbid schizophrenic patients, bipolar depressive patients, and unipolar depressive patients are compared to determine whether lateralized temporal lobe dysfunction is characteristic of a specific diagnostic subgroup of patients.

Ehrhardt, Anke A., and Meyer-Bahlburg, Heino F.: Child Psychiatry, Psychoendocrinology. An interdisciplinary pilot study is concerned with the impact of somatic and hormonal changes of puberty on the mental health of the early adolescent, as well as basic questions about the hormone/behavior relationships in this developmental phase. The sex hormone dependency of psychopathology and mood, sexual and gender role behavior, and cognitive sex differences are examined in relative isolation from environmental factors that usually coincide with puberty.

Shaffer, David: Child Psychiatry, Neuropsychiatry. The relationships between neurological soft signs and psychiatric disorders are studied. Subjects are young black males who were identified at age 7 as having neurological soft signs. A considerable amount of neonatal and developmental data are available on these subjects, who were originally studied as part of the National Collaborative Perinatal Project, a prospective study of pregnancy and pregnancy outcome. The teenagers undergo psychiatric, neurological, cognitive, and scholastic attainment assessments.

In 1980, the computer and biometric assessment facilities and the psychoendocrinology and neuropsychiatry research projects with adolescent subjects continue to receive National Institute of Mental Health support.

Adolescents and young adults with a history of very early or precocious puberty are examined in the psychoendocrinology project. The studies are designed to determine the influence of precocious puberty on psychosexual development, affective experience, cognitive development, and hemispheric lateralization. The psychological development of children with prenatal diethylstilbestrol (DES) exposure and children with major birth defects of the sex organs is also investigated. In addition, hypogonadal females and individuals with Turner's Syndrome are studied.

The neuropsychiatric study of black males with neurological soft signs is expanded to include black females and white adolescents of both sexes. In addition, febrile convulsions in childhood are analyzed. One project concerned with the natural history of these convulsions, emphasized neurological, psychiatric, and cognitive outcome. Two other studies are designed to examine the effects of anticonvulsants on behavior and cognition. One study is a double-blind trial involving children who have had two febrile seizures; the other study is concerned with medication withdrawal in epileptic children who have been free of seizures for 1 or more years.

Two projects receive initial funding in 1980:

Puig-Antich, Joaquim: Neuroendocrine Sleep Physiology Laboratory. A new facility provides for the study of relationships between sleep physiology—as measured by the electroencephalogram—and circadian hormone secretion rhythms in normal and psychopathological states. The facility is used in research with children, adolescents, and adults with a variety of psychiatric disorders.

Puig-Antich, Joaquim: Adolescent Depression and Conduct Disorder. A study is designed to test the hypothesis that adolescents who simultaneously meet the diagnostic criteria for major depressive disorder and conduct disorder will show amelioration or cessation of symptomatic behavior in both diagnostic areas in response to treatment with imipramine for a period of 3 months.

Effect of Psychotherapy in Schizophrenia
MH 26183; $209,986

Knapp, Peter H.
University Hospital
Boston, MA

A collaborative pilot program to evaluate intensive psychotherapy for treatment of hospitalized schizophrenic patients is conducted. Two hospitals in the Boston area, McLean and Boston State, are participating in this study. Patients are randomly assigned to an intensive psychotherapy treatment program, and a control group receives treatment in the general hospital psychiatric treatment program. A number of baseline measures taken during treatment and on a followup basis are used to assess the outcome. The traits of a therapeutically effective clinician are identified.

Beginning in 1978, primary efforts were aimed at maintaining uniformity of conditions for this collaborative comparison of treatment of hospitalized schizophrenic patients by intensive psychoanalytic therapy or treatment as usual. The collaborative study is P01 MH 005246.

Research in Autism: Parent Intervention
MH 28210; $64,483

Koegel, Robert L.
University of California
Santa Barbara, CA

An assessment is made of the effect of parent training in behavior modification as a method of improving the treatment of autistic children. Emphasis is on defining the differential effects from a group of parents trained in behavior modification techniques who treat their autistic children, versus standardized treatment in a clinical setting for a control group of autistic children. Approximately 72 autistic children are in the sample. Some are treated at the University of California in Santa Barbara. Others are treated in a collaborative program (R01 MH028231) under the direction of Laura Schreibman at Claremont Men's College, Claremont, California. Exhaustive data are collected for both the parents and the autistic children. For the experimental parent training group, the child's entire treatment is conducted by his parents, who are instructed in behavioral modification methods. The control group is given direct clinical treatment. Additional data are collected every 3 months. Followup data are collected 6 months and 4 years after termination of treatment.

Neuropsychopharmacological Studies of Attention
MH 12568; $94,784

Kornetsky, Conan
Boston University
Boston, MA

Human and animal studies examine the relationship of subcortical changes affecting attention to perception in schizophrenia and petit mal epilepsy. Cortical and subcortical sites concerned with impaired attention in behavioral tasks are identified. The effects of intracranial self-stimulation (ICSS), changes in ICSS threshold, microapplication of neurotransmitters, brain lesions, and centrally acting drugs (chlorpromazine, secobarbital, amphetamine) and their interaction on attention, electroencephalogram (EEG), and motor and sensory reactions are analyzed. The relationship between visual perceptual changes and EEG pattern are studied in experimental petit mal in animals and in human epilepsy patients, schizophrenics, alcoholics, hyperactive children, and high-risk children of psychotic mothers. The effect of prenatal trauma (maternal hypoxia, central brain stimulation, drug intoxication with phenothiazines, barbiturates, tetrahydrocannabinol, adrenergic and cholinergic drugs) on attention and cognition, the EEG and evoked potential, central nervous system pathology, and steroid and catecholamine composition are examined in rats and monkeys. An analysis of the mechanisms of single dose tolerance to morphine in the rat and the effect of naloxone is undertaken, and EEG studies of single and multiple doses of morphine are extended to other drugs of abuse.

Mental Health Clinical Research Center for the Study of Schizophrenia
MH 30911; $41,709

Liberman, Robert P.
University of California
Los Angeles, CA

The Mental Health Clinical Research Center for the Study of Schizophrenia has a program which encompasses several basic research and clinical issues in schizophrenia, especially chronic schizophrenia. The program, which is at the Camarillo Neuropsychiatric Institute Research Center in Camarillo, California, represents a joint effort between the University of California at Los Angeles, Department of Psychiatry, and Camarillo State Hospital. This grant supports major research projects aimed at gaining information relevant to prevention of relapse and rehospitalization in schizophrenic patients.

Aitchison, Robert: Home-based Behavioral Observation of Interaction Within the Families of Schizophrenics. This study is subsumed under the Family Factors in Schizophrenic Relapse project. It is concerned with developing, validating, and utilizing naturalistic observation codes to study sequences consisting of appropriate or inappropriate patient behavior in the home and the parental reaction to that behavior. A study is made of the similarity of patients' behavior when they are observed in simulated family interaction used at the hospital to assess progress in therapy with the same interaction behaviors when assessed directly in the patients' homes. The project is also concerned with examining changes in patient interaction/communication skills after discharge and developing Family Training Packages to reduce relapse by teaching families how to maintain effective social and family living skills. The patients in this research are between 18 and 35 years of age.

Liberman, Robert: Social Skills Training for Relapsing Schizophrenics. This study assesses the relative effectiveness of social skills training in preventing the relapse and rehospitalization of schizophrenic patients. Social skills training consists of a set of standardized role playing situations in which the patient must show competence as a receiver, processor, and sender of interpersonal messages in each situation before he can proceed to the next situation. Training techniques include behavior rehearsal, role playing, prompting, instructions, modeling, and contingent reinforcement. The effectiveness of social skills training is assessed with and without medication, and contrasted with the effectiveness of another treatment program which also utilizes individually determined doses of antipsychotic medication. Patients in this study are males between the ages of 18 and 35 years who are considered at high risk for relapse.

Vaughn, Christine: Family Factors in Schizophrenia Relapse. This study is a replication of some English studies. The Camberwell

Family Interview is standardized on American subjects, ratings of the expressed emotion of key relatives are derived from it, and the relationships between these ratings and patient symptomatic relapse are studied. The ratings of expressed emotion have three components: a component relating to critical comments made by the relative when talking about the patient and his illness, a component relating to hostility, and a component relating to emotional overinvolvement. Additional project objectives are to identify the coping skills used by relatives and significant others to deal with patient illness behaviors, and to identify those patient behaviors or impairments viewed as most disturbing by the relatives.

In 1979, the Mental Health Clinical Research Center for the Study of Schizophrenia conducted four research projects. It has also provided research training on an apprenticeship basis for individuals at different levels of academic achievement and personnel training in the social skills area at the regional and national level. The research projects are:

Goldstein, Michael: Family Communication and Affect in Schizophrenic Relapse. This study focuses on two measures developed to assess the communication of the significant others associated with persons who develop schizophrenic symptoms or who show a recurrence of these symptoms after discharge. The measures are the Goldstein/Rodnick Communication Deviance Index and the Vaughn and Leff Expressed Emotion Scale developed from the Camberwell Family Interview. The aim is to investigate the relation of these measures to each other and to direct observational measures. A second goal is to assess the ability of each of these measures to predict the relapse of patients hospitalized for schizophrenia.

Karno, Marvin: The Course of Schizophrenia Among Mexican-Americans. The relationship between a patient's relapse and the level of a key relative's expressed emotion, as measured by the Camberwell Family Interview, is studied in a group of Mexican-Americans. Familial and patient compliance with the maintenance of antipsychotic medication and recommended followup care is also investigated. Utilization of forms of social support which may affect illness outcome are considered.

Marder, Stephen R.: Predicting Optimal Neuroleptic Therapy for Schizophrenic Outpatients. Eighty schizophrenic outpatients are treated in a double-blind comparison of two doses of fluphenazine decanoate, which are administered every 2 weeks. The initial injection is treated as a test dose. Pharmacokinetic, biological (prolactin level, assay for dopamine binding), neurophysiological (computerized electroencephalogram), and clinical information is collected at intervals during the 14 days following the test dose. An analysis is performed to determine whether information collected just after the test dose predicts subsequent treatment outcome. Extrapyramidal symptoms and tardive dyskinesia are monitored using clinical ratings and a recently developed tremor analyzer.

Wallace, Charles J.: Development Processes in Schizophrenic Relapse. This longitudinal research, focused on relapse and remission, has the aim of identifying classes of variables related to the clinical course of schizophrenia. A multilevel battery of measures are taken during the first hospitalization, 1 or 5 months after initial assessment, and every 6 months thereafter, for 5 years. The following assessment categories are utilized: psychopathology, social skills, instrumental role skills, Camberwell Family Interview, direct behavioral observation, psychophysiology (electrodermal), cognition/attention, and life history/participant observation.

Experimental Studies in Child Schizophrenia
MH 11440; $37,497

Lovaas, O. Ivar
University of California
Los Angeles, CA

A treatment program based upon learning theory principles is developed for autistic children. The research is concerned with isolating the kinds of environmental variables which control the strength of psychopathological behaviors, including self-destruction, echolalia, and self-stimulation, in severely psychotic (autistic and schizophrenic), mute, and echolalic children. It is also concerned with establishing programs for the acquisition of imitative behavior, particularly in the area of speech, and with the establishment of abstract speech. The effectiveness of behavior modification for very young children is assessed. In addition, basic research is concerned with overselective attention (stimulus overselectivity), the extent to which autistic children experience a restriction in the number of stimulus elements in a complex input which acquires functional control over their behavior. Stimulus overselectivity is investigated across and within sensory modalities, in social situations, and as related to intelligence quotient (IQ) levels in retardates and chronological age in normal subjects. The extent to which stimulus overselectivity interferes with prompt fading procedures, stimulus generalization, and observational learning is assessed. The research is also concerned with the isolation and development of new sources of motivation, as in sensory and perceptual reinforcement.

In 1980, behavioral treatment continues to be offered to young autistic children (children less than 46 months of age if echolalic, 40 months of age if mute). The children have been assigned to two groups—a treatment group receiving more than 40 hours of treatment per week, and a treatment group receiving less than 40 hours per week. Treatment includes parent training. Pretreatment assessment includes psychiatric and neurological evaluations, psychological testing, behavioral recording, diagnostic checklists, and other assessments. Posttreatment measures are carried out after the child has reached 6 years of age and include the child's ability to function independently in, adequately adjust to, and learn from normal school placement.

National Institute of Mental Health/World Health Organization Study on the Determinants of Mental Disorders
MH 31016; $36,720

Marsella, Anthony J.
Queen's Medical Center
Honolulu, HI

A Hawaiian research group is participating as a United States field research center in the National Institute of Mental Health/World Health Organization study of the causes, courses and outcomes of mental disorders. Emphasis is on psychosocial aspects (life stresses, family morbidity, family interaction processes and communication, and social deviance) of schizophrenic disorders among Caucasian-American, Hawaiian-American, and Japanese-American populations in Hawaii.

Theoretical Research in Psychiatry and Neurobiology
MH 00108; $39,010

Matthysse, Steven W.
Harvard Medical School
Boston, MA

Four research projects have as their common theme the use of mathematical and theoretical analysis to study problems in psychiatry and neurobiology. In the first project, rhesus monkeys are maintained on amphetamine, and effects on disattentional behavior are examined. Disattention is defined as the adaptive ability of an organism to withdraw his attention from a stimulus after having attended to it. The second project relates to the foundation of quantum mechanical molecular structure calculations and involves an attempt to more rigorously calculate the probability of various molecular configurations of psychoactive drugs. The third project is concerned with an evaluation of a two-gene model for schizophrenia. The fourth project concerns developing a theory for describing the rotational, translational, and kinetic fluctuations in the lipid protein matrix of cell membranes.

Monoamine Oxidase, Dopamine Beta-Hydroxylase, and Adenosine Triphosphatase Activities in Psychosis
MH 25116; $103,038

Meltzer, Herbert Y.
University of Chicago
Chicago, IL

Patients with various types of functional psychoses—primarily schizophrenia and affective disorders—and normal controls participate in studies of enzyme activities. The research focuses on monoamine oxidase (MAO) patterns in blood platelets and skeletal muscle; dopamine β-hydroxylase (DBH) patterns in the serum and the sympathetic nerves in skeletal muscle; and the activities of magnesium, potassium, and sodium adenosine triphosphatases (ATPases) in erythrocyte membranes. The effects of psychoactive drugs (chlorpromazine, promethazine, chlorperazine, perphenazine, and other compounds) on enzyme activities is monitored in patients and in laboratory rats. Pilot studies are carried out on tissues obtained at autopsy from psychotic patients. Tissues studied include skeletal muscle, liver, stellate ganglia, and adrenal medulla. An attempt is made to correlate clinical status with the psychopharmacological and historical data. The results of the studies are examined in light of other research on neurogenic abnormalities in skeletal muscle, abnormalities of terminal motor nerves, and elevated serum creatine phosphokinase activity.

In later studies beginning in

1978, techniques in the use of chemical methodology and thorough clinical evaluation are refined to assess the relationships between potentially important biological indicators and clinical symptomatology.

Clinical Research Center for the Study of the Major Psychoses
MH 30938; $427,467

Meltzer, Herbert Y.
University of Chicago
Chicago, IL

A mental health clinical research center is established for the multidisciplinary longitudinal study of the biological and behavioral factors associated with the major psychoses: schizophrenia, affective psychoses, and mixed states. Emphasis is on standardized diagnostic assessment based on established interview schedules, assessment of clinical change, and longitudinal followup of subjects. Neuroendocrine, biochemical neuropsychologic, morphologic, psychopharmacologic, pharmacokinetic, and psychological studies are conducted on clinical populations. Clinically relevant basic research, particularly in the area of neuroendocrinology, is also emphasized.

Meltzer, Herbert Y.; Schyve, Paul: One group of investigators concentrates on the diagnosis, phenomenology, and followup studies of clinical populations. A number of biochemical and neuroendocrine investigations are performed. A series of laboratory studies are done with animals.

Davis, John; Garver, David: Other areas of concentration are clinical investigations of depression and schizophrenia concentrating on psychopharmacologic, pharmacokinetic, and genetic studies. Included is basic research studying the effects of amphetamine and phencyclidine in animals. Overall objectives are clarification of the most efficient use of psychopharmacologic agents as well as the development of clinically useful tools for predicting drug response.

Crayton, John; Tamminga, Carol: In still another area, many investigations are made of neuroendocrine and neuromuscular dysfunction in institutionalized, treatment-resistant, chronic schizophrenics. Studies are also conducted on tardive dyskinesia via the use of measurements of the clinical effects of choline, clozapine, and muscimol.

Halaris, Angelos: In another setting, studies are made of the blood levels of monoamine metabolites in depression, pharmacotherapy of depression, and serotonin levels in autistic children.

Neuromuscular Dysfunction in the Psychoses
MH 47808; $39,107

Meltzer, Herbert Y.
University of Chicago
Chicago, IL

Biochemical and neuroendocrine studies of the psychoses, especially schizophrenia and affective disorders, are conducted in clinical populations. Platelet monoamine oxidase, and serum creatinine phosphokinase, cortisol, or dopamine β-hydroxylase levels are measured and correlated with neuromuscular dysfunction or with clinical states. Alterations in serum prolactin after neuroleptic drug administration are also examined. A series of studies in laboratory animals examines endocrine and neurotransmitter response to drugs, including phencyclidine.

Community Alternatives for Treatment of Schizophrenia
MH 20123; $143,274

Menn, Alma Z.
Mental Research Institute
Palo Alto, CA

A comparison is made of the relative effectiveness of two treatments of first admission, acute, young schizophrenics. One is residential treatment in a community residence, called Soteria House, which is staffed mostly by nonprofessionals. Here, staff behavior stems from a philosophy that a psychosis may be a potential growth experience. Extensive and intensive interpersonal contact is maintained, while use of medical or other physical therapies is avoided as much as possible. Subjects are between the ages of 16 and 30, unmarried or divorced or separated. Treatment evaluation is based on open-ended self-reports, the Moos Ward Atmosphere Scale, and an independent sociologist's field study. Followup is done at intervals for 2 years. Control data are gathered for a similar group of patients treated in the usual manner in a community health center.

Preliminary data have been collected by December 1978. A new comparative outcome study with an improved research design utilizing about 50 experimental and 50 control patients is in the process of completion. Admission, discharge, 6, 12, and 24 month postadmission data from a variety of measures which assess outcome in terms of symptoms, levels of psychosocial functioning, and quality of life are compared across groups. Short-term and long-term cost/benefits are compared, and characteristics of subgroups of responders and nonresponders to the different treatments are identified.

Studies in the Neuropsychology of Attention
MH 14915; $22,545

Mirsky, Allan F.
Boston University
Boston, MA

The neurophysiological and behavioral correlates of attention are studied. Using monkeys and rats as subjects, the investigator examines the electrical brain-stimulation-induced alterations in attentive behavior; studies the visual system with particular emphasis on the activity of the efferent pathway to the retina and its relation to the central events in petit mal epilepsy; explores the possible role of altered prenatal or perinatal events in the development of the pathophysiology of petit mal epilepsy and other disorders in which altered subcortical structures play an etiologic role; and to investigate the disease mechanisms of young epileptic animals in which impaired attention appears to be a significant symptom.

Human studies include an investigation of the attention processes of high-risk children, ages 5–12, who have schizophrenic mothers, and children with infantile autism. Monkeys deprived of oxygen during gestation show some sensory and attentional deficits, and this model is compared with the behavior of autistic children. Evoked sensory potentials, far-field brainstem activity, and electroretinograms are examined in epileptic patients during petit mal seizures. A prosthetic sensory stimulation device for predicting or ameliorating petit mal seizures is developed.

Adjustment of Children of Schizophrenic Parents
MH 21145; $67,081

Neale, John M.
State University of New York
Stony Brook, NY

Assessment is made of the social and academic adjustment of high-risk, school-age children of schizophrenic, depressed, and normal parents. The data are divided into three parts: a detailed assessment of the mental status and social history of both parents and the family as a whole; descriptive information on the academic history and on the social adjustment of the children as viewed by parents, teachers, and peers; and the experimental study of current theories regarding schizophrenia.

The longitudinal study continued in 1978 follows up on the development of the subjects to determine which evaluated characteristics of the children, parents, and families are stable over prolonged periods of time.

Attributions and Helplessness in Clinical Depression
MH 31640; $61,409

Norman, William H.
Butler Hospital
Providence, RI

Three studies are aimed at investigating the applicability of the learned helplessness model of depression to clinically depressed patients. Learned helplessness refers to deficits in the performance of a reinforced task noted in subjects who were originally trained on a task in which responses were independent of outcome. In the first study, 45 clinically depressed patients, 45 improved depressed patients, and 45 nondepressed patients are studied with regard to learned helplessness and attributions for their failures. In the second study, the occurrence of learned helplessness is studied in 120 subjects from the following diagnostic groups: primary affective disorder, secondary affective disorder, nondepressed schizophrenia, and nondepressed other disorder. The third study determines the relative efficacy of two treatment interventions developed from learned helplessness models. The study involves 160 acutely depressed inpatients who are randomly assigned to four groups: reattribution training, contingent success, combined reattribution and contingent success, and waiting period control group.

Electrophysiologic Studies of Autism
MH 35239; $19,700

Novick, Barbara
Yeshiva University
Bronx, NY

Disorders in neural processing are identified in autistic children by studying event-related potentials. One hypothesis is that neurophysiological defects exist at several stages of auditory and visual information processing and underlie behavioral disturbances associated with autism. Another hypothesis is that the number of processing defects and their distribution in specific processing stages differ from one child to the next, and result in idiosyncratic patterns of neurophysiological deficits that underlie the diverse clinical manifestations of autism. Subjects are normal and autistic children, 6 to 16 years of age.

Cognition, Speech, and Vulnerability to Schizophrenia
MH 31536; $71,747

Oltmanns, Thomas F.
University of Indiana
Bloomington, IN

Two longitudinal studies are designed to clarify the role of cognitive difficulties in vulnerability to schizophrenia. The goal of the studies is to determine if the cognitive problems investigated are stable characteristics specific to schizophrenic individuals or transient epiphenomena associated with severe psychiatric disturbance in general. The studies utilize several measures related to short-term memory processes, including sentence comprehension, short-term recall, and referential communication. The first study involves testing groups of schizophrenic, manic, unipolar depressive, and nonpsychiatric patients (from the Veterans Administration Hospital in Indianapolis) upon admission to the hospital and again when they are discharged. In the second study, similar groups of outpatients who are in remission are tested at successive 6-month intervals.

Developmental Psychophysiology of Attention
MH 00054; $15,660

Porges, Stephen W.
University of Illinois
Champaign, IL

An attempt is made to develop a comprehensive psychophysiological model of attention. Biological indices are developed for both short- and long-term attentional processes which can be used in basic and applied research. The primary biological measures are heart rate and respiration. Investigations are made of heart rate variability as an index of sustained attention. An attempt is made to differentiate the two components of the attentional process—the involuntary (or reflexive) and the voluntary (or instrumental). It is the voluntary component which is characterized by stabilization of the heart rate. This component is concordant with the stimulus processing associated with voluntary sustained attention. The hope is to understand the relationship between physiological responses and attention in the normal adult and to study this relationship along a developmental continuum. The use of normal (newborn through college age) and pathological populations (e.g., hyperactive children, autistic children) is a means of applying the findings from normal development to identify developmental pathologies.

Hormones in Cause and Treatment of Affective Disorders
MH 22536; $40,923

Prange, Arthur J., Jr.
University of North Carolina
Chapel Hill, NC

Under investigation is the role of biological factors in the cause, perpetuation, relapse, and treatment of affective disorders, particularly depression. The therapeutic value of thyrotropin-releasing hormone is investigated in depressed women, depressed men, manic patients, schizophrenics, and hyperkinetic children. Systematic trials are conducted to determine whether small doses of testosterone accelerate the antidepressant action of imipramine in men without precipitating a delusional syndrome. In animals, behavioral and biochemical studies are directed at elucidating the central actions of thyrotropin-releasing hormone and other hypothalamic-releasing factors. Clinical studies are carried out at the Dorothea Dix Hospital in Raleigh, North Carolina, and North Carolina Memorial Hospital in Chapel Hill.

In later years, studies are addressed to an exploration of the behavioral effects of thyrotropin-releasing hormone, luteinizing hormone-releasing hormone, and neurotensin in animals, and of thyrotropin-releasing hormone in man. In animals, mechanisms of action are explored, in addition. In man, relationships between the hypothalamic/pituitary/thyroid axis and the hypothalamic/pituitary/adrenal axis are also studied. Human subjects include schizophrenic patients, depressed patients in remission, and alcoholics in remission.

Mental Health Clinical Research Center for Psychoendocrinological Studies of Mentally Ill Children and Adults
MH 33127; $145,594

Prange, Arthur J., Jr.
University of North Carolina
Chapel Hill, NC

A Mental Health Clinical Research Center is established to study the neuroendocrinological and psychoendocrinological aspects of the major mental disorders, which form the core of mental health problems. The Center includes a clinical component, located primarily at the Dorothea Dix Hospital in Raleigh, and a basic science component, located on the University of North Carolina campus. It also includes a biostatistics section, which provides statistical support for all aspects of research performed in the Center.

Clinical studies of the Center include the following:

Loosen, Peter T.: Psychoendocrinology in Adult Mental Illness. These studies relate to behavioral changes in selected endocrine disturbances, endocrine changes observed with behavioral disturbances, and behavioral changes following hormone administration. Studies concerned with the thyroid-stimulating hormone (TSH) response to thyrotropin-releasing hormone (TRH) are performed utilizing normal male subjects, patients with depressive and manic illnesses, relatives of depressed patients, patients with delirium tremens, and abstinent alcoholics. Biorhythm studies related to TSH and cortisol are performed with schizophrenic patients.

Gualitieri, Thomas C.: Psychoendocrinology in Childhood Mental Illness. Pilot research is concerned with pituitary hormones in child psychiatry patients.

Elston, Robert E.: Genetic Studies. Pilot research relates to identifying and mapping genes in patients with depressive spectrum diseases or blunting of TSH response to TRH injection.

Burnett, Gordon: Psychoendocrinology in Renal Dialysis Patients. Neuroendocrine, neuropsychological, and psychiatric interview data from renal dialysis patients are gathered and interrelated.

Basic studies performed at the Center include the following:

Kizer, John S.: Neuroendocrine Studies. Pilot research on the neuronal pathways to the medial basal hypothalamus is performed.

Youngblood, William: Analytical Biochemistry. Radioimmune assay techniques are developed to determine levels of neuropeptides (including endorphin, enkephalin, and hypothalamic-releasing factors) in blood and urine of rats and humans (including depressed patients) and in various areas of the rat brain. Brain TRH distribution and sites of action are also examined in rats.

Breese, G.R.: Neuropharmacology. Pilot research is concerned with the mode of action of antipsychotic drugs.

Prange, Arthur: Behavioral Pharmacology. Pilot research investigates the functional roles, mechanisms, or sites of action of TRH and neurotensin.

Epidemiological Genetics and Family Study
MH 31302; $299,619

Reich, Theodore
Washington University
University City, MO

A mental health clinical research center has a program of research focusing on the ways in which genetic and environmental factors interact in the families of psychiatrically ill individuals and effect the transmission of a disorder from one generation to the next. Major projects include:

Anthony, E.J.: Establishing a Family Research Center at a Large State Hospital. A pilot study is concerned with investigating the role of adolescent turmoil in adolescent affective disorders and schizophrenia, and with determining the relationship of adolescent turmoil to familial psychiatric disturbance.

Cloninger, R.C.: The Analysis of Multivariate Models of Diagnosis, Prognosis, and Familial Resemblance in Psychiatry. Multivariate methods for parameter estimation and hypothesis testing are studied. Computer programs are implemented and documented. Diagnostic reliability, followup data, and family data are combined into a single analytic structure, so that the extent to which these variables interact can be measured.

Fishman, P.: Detection of Linkage for Critical Genes. A new method for the detection of critical genes in the transmission of a psychiatric entity is developed and implemented. The methodology is relatively free of assumptions in that the genetic mechanism for the transmission of the disorder is not specified before the analysis is carried out. The method is applied to families with an individual with a manic-depressive illness. In addition, an attempt is made to detect genetic linkage between well-established genetic markers and Alzheimer's dementia.

Helzer, J.E.: Application of Computer Based Interview for Routine Examinations of Psychiatric Patients. A pilot project is concerned with automating routine patient information to improve patient care and facilitate research.

Martin, R.: The Genetics of Alzheimer's Dementia, Presenile and Senile. The genetic transmission of Alzheimer's disease is studied, and psychometric measurements of patients and relatives are obtained and analyzed.

Reich, T.: Genetic and Family Studies. Models of disease transmission and analytic methodologies which are applicable to psychiatric disorders are extended and implemented. The methods developed are to be applied to data obtained from the studies of children of manic-depressive and schizophrenic parents, and the families of individuals with Alzheimer's disease.

Robins, L.N.: Developing Reliable Assessments of Early Family Environment. Patients with unipolar depressive illness and substance abuse problems, and the families of these patients, are studied to develop reliable measures of early family environment which may aid in the understanding of familial, nongenetic precursors or causes of mental illness.

Wetzel, J.L.: A Community Study of the Relationship Between Anxiety and Depression. Preliminary research is concerned with the development of an urban survey which will be useful in comparing relatives of psychiatrically disordered and nonpsychiatrically disordered subjects in terms of prevalence rates of similar or nonsimilar disorders. The survey is also designed to clarify the relationships among symptoms, syndromes, and measures of anxiety and depression.

Neurobiological Basis of Major Psychiatric Disorders
MH 25642; $432,093

Reiser, Morton F.
Yale University
New Haven, CT

This collaborative work involving basic neurobiological research and clinical testing explores neurobiological factors in the genesis and treatment of major psychiatric disorders. The basic science section of the program includes study of central neurotransmitters, receptors, and drugs as well as study of neurobiological processes in behavior. The first phase investigates the effects of drugs that are of major importance in psychiatry—including antipsychotic and antidepressive drugs—on central neurotransmitters, primarily monoamines and acetylcholine. The basic neurobiological aspect of the program, which provides for development of anatomical, histochemical, biochemical, and neurophysiological techniques, forms an essential groundwork for the behavioral studies. The major subdivisions of the clinical investigations, involving human subjects, include biological processes which may be related to the genesis of schizophrenia and the affective disorders and biological predictors of treatment response in these kinds of disorders. Anxiety and aggression are also investigated. Experimental animals are rats, cats, and monkeys.

Low Dose Neuroleptic Medication in Schizophrenia
MH 33814; $57,223

Rifkin, Arthur E.
Mount Sinai School of Medicine
New York, NY

The efficacies of minimal or standard dose levels of fluphenazine decanoate in long-term treatment of schizophrenic outpatients are compared. Factors such as symptoms of schizophrenia, side effects from the drug, rates of relapse, amount of rejection of medical regime, restabilization, social adjustment, life stress, and perceived burden on the patient's family are assessed for the two dose levels.

Genetic and Immunohematologic Factors in Autism
MH 31274; $81,220

Ritvo, Edward R.
University of California
Los Angeles, CA

A series of hypotheses that genetic factors are significant in the etiology of certain aspects of childhood autism are tested. Research and studies include: family histories for neurological and psychiatric illness and developmental disabilities; Behavioral Observation Scale data; morphologic and dermatoglyphic measures; chromosome studies including gene markers and differential bandings; histocompatability factors of peripheral blood lymphocytes; family profiles of blood serotonin and platelet counts; and prevalence of allergic diseases and assessment of the immunologic systems. Subjects include 50 autistic children, 200 family members, 25 control cases, and 100 control family members for a total of 375 participants. In addition, 30 families with one autistic child and 20 multiple case families, in which 10 are twins and 10 are not, are studied.

Role of Monoamine Oxidase in Schizophrenia
MH 34757; $196,393

Rose, Robert M.
University of Texas
Galveston, TX

Platelet monoamine oxidase (MAO) is studied in schizophrenic and schizoaffective patients. The research, now in the pilot phase, has three components: biochemical studies, cross-sectional clinical study, and longitudinal clinical study. Biochemical studies are concerned with purifying the enzyme, examining its kinetic properties with different substrates and inhibitors, and assessing its structure through electrophoretic assays and immunoassays with monospecific and monoclonal antibodies. The clinical study is concerned with differences between schizophrenic spectrum patients and normal control subjects in the amount or structural properties of the enzyme. In addition, the relationships between MAO measures and illness factors (such as prognosis, chronicity, paranoia, drug therapy, hospitalization, symptom clusters, and demographic variables) are investigated. The longitudinal clinical study determines relationships between platelet MAO measures, clinical change, and neuroleptic drug effects. Patient populations are recruited from the University of Texas Medical Branch in Galveston and from Austin State Hospital in Austin, Texas.

Late Event Related Potentials in Psychiatric Patients
MH 35330; $86,974

Roth, Walton T.
Stanford University
Stanford, CA

The meaning of the reduced amplitude of the P300 brain wave in schizophrenia is studied. A series of experiments with normal and schizophrenic subjects test hypotheses regarding the following possible causes of reduction of this late positive component of the event-related potential in schizophrenia: deficits in selective attention, failure to apprehend sequential probability, general loss of reactivity, and poor reaction time performance. A second series of experiments, utilizing patients with major depressive disorder in addition to normal and schizophrenic subjects, tests hypotheses concerning P300 and diagnostic categorization, affective reactivity, and formal thought disorder. The effects of increasing stimulus complexity on P300 are investigated.

Steroid Hormones in Depressive Illness
MH 29841; $214,321

Sachar, Edward J.
Columbia University
New York, NY

The production and excretion of steroid hormones, particularly sex hormones, during the course of depressive illness are studied. Subjects are males, age 30 to 64, and females, age 42 to 62, who are hospitalized for psychotic depressive, manic-depressive (depressed state), or involutional psychotic reactions.

The use of neuroendocrine techniques to study altered brain function in psychiatric disorders is continued in 1978. Subjects include depressed adults, depressed prepubertal children, and adults in remission from depressive illnesses, with and without lithium prophylaxis. Schizophrenic patients; patients with hyperparathyroidism; school-aged, hyperkinetic children; acutely bereaved adults; and normal subjects are also studied.

In 1981, the extent of abnormal neuroendocrine function in depressed patients continues to be examined. Studies with depressive and control subjects include assessments in circadian patterns of cortisol, human growth hormone and prolactin secretion; cortisol response to dexamethasone and atropine; diurnal hormone responses to amphetamine, desipramine, and fenfluramine; and thyroid-stimulating hormone response to thyroid-releasing hormone. Hormonal responses to drugs are analyzed for implications for neurotransmitter mechanisms. In addition, the relation between prolactin secretion—as an index of dopamine blockade—and relapse rate is studied in remitted schizophrenics maintained on very low neuroleptic dosage. Hormonal and behavioral responses to amphetamine are compared in typical schizophrenics and schizophrenics with histories of childhood asociality. Prolactin responses to haloperidol and dopamine are investigated in neuroleptic-resistant and neuroleptic-responsive schizophrenics.

Determinants of Outcome of Severe Mental Disorder
MH 29969; $250,000

Sartorius, Norman
World Health Organization
Geneva, Switzerland

A cross-cultural investigation is made of the elements in the social structure which contribute to or assist in stemming chronicity in schizophrenia. The focus is on the family—the social content common to all cultures; an intensive study is made of its environmental and interactive role with the course of psychosis. Data are gathered in 11 field research centers in nine countries. The centers are located at: Cali in Colombia, Prague in Czechoslovakia, Ararhus in Denmark, Nottingham in England, Agra and Chandigarh in India, Nagasaki in Japan, Ibadan in Nigeria, Moscow in Russia, and Honolulu, Hawaii, and Rochester, New York in the United States. Various psychological, sociological, and anthropological techniques are used to study possible differences, within each country, of family reactions to a schizophrenic breakdown in a family member. Attempts are made to refine predictors of course and outcome using multiple analysis of initial and followup data. Each field research center has a sample of 80 to 100 index cases, with the same number of index and control family units. Total population under study consists of 800 to 1,000 schizophrenic patients and 1,600 to 2,000 family units.

Psychopharmacology of Biogenic Amines in Depressions
MH 15413; $210,356

Schildkraut, Joseph J.
Harvard Medical School
Boston, MA

An integrated program of clinical and pharmacological research explores the underlying biochemical pathophysiology of the affective disorders, as well as the possible mechanisms of action of drugs (and other somatic interventions) used in their treatment.

The research can be subsumed under several broad categories: studies of biological differences in clinically defined subtypes of depressive disorders; studies of the clinical differences in groupings of depressed patients defined by various biological criteria; studies of the relationships among various biological variables in patients with depressive disorders; and studies of pretreatment biological and clinical variables as predictors of response to antidepressant pharmacotherapy.

Other projects include longitudinal studies of changes associated with drug administration or changes in clinical state in patients with depressions or manias; studies of the changes in norepinephrine turnover in the rat brain after acute and chronic administration of lithium salts, electroconvulsive shock, or tricyclic antidepressant drugs; and the relation of biogenic amine metabolism to sleep stages. Subsequent research includes biochemical classifications of the schizophrenias as well as the affective disorders, investigating the relation of biogenic amines and other biochemical factors to other clinical diagnostic criteria.

In 1981, the project continues to focus on investigating the noradrenergic basis of depression with studies into baseline levels of platelet monoamine oxidase and urinary methoxyhydroxyphenylglycol (MHPG) as predictors for responses to antidepressant drugs.

Research in Autism: Parent Intervention
MH 28231; $68,389

Schreibman, Laura E.
Claremont Men's College
Claremont, CA

An assessment is made of the effect of parent training in behavior modification as a method of improving the treatment of autistic children. Emphasis is on defining the differential effects from a group of parents trained in behavior modification techniques who treat their autistic children, versus standardized treatment in a clinical setting for a control group of autistic children. Approximately 72 autistic chilren are in the sample. Some are treated at the Claremont Men's College in Claremont, California. Others are treated in a collaborative program (R01 MH 028210) under the direction of Robert Koegel at the University of California at Santa Barbara. Exhaustive data are collected for both the parents and the autistic children. For the experimental parent training group, the child's entire treatment is conducted by his parents, who are instructed in behavioral modification methods. The control data are collected every 3 months. Followup data are collected 6 months and 4 years after termination of treatment.

Electrophysiological Studies of Psychiatric Disorders
MH 12507; $156,106

Shagass, Charles
Temple University
Philadelphia, PA

The aim of this research is to increase understanding of the neural mechanisms underlying various kinds of psychopathology. The studies focus upon establishing psychopathological correlates of electrophysiological events, which can be recorded by noninvasive procedures from the human scalp, such as evoked potentials and the electroencephalogram. All the major diagnostic categories are studied, but special emphasis is placed on the schizophrenic and affective psychoses. Although most of the research utilizes human subjects, some animal research was performed in the early years of the grant.

In 1979, impedance plethysmography or rheoencephalography was utilized to obtain indices of regional cerebral blood flow. Research efforts are directed toward: confirming and extending findings showing deviant patterning and topography of evoked potentials in psychiatric illness; determining correlations between event-related potentials and rheoencephalogram measurements; confirming deviant slow-potential findings in psychosis; testing attention deficits in schizophrenia and affective psychoses; and testing hypotheses relating to contingent negative variation. Clinical populations, particularly patients with schizophrenias, affective disorders, personality disorders, and neuroses, are compared with one another and with nonpatients.

Object Concepts in Autistic Children
MH 33815; $67,497

Sigman, Marian
University of California
Los Angeles, CA

The object concepts of children with infantile autism are investigated. Categorization of objects as manifested in sorting, functional, and symbolic use of objects in play, and sensorimotor behaviors thought to reflect object permanence—the knowledge that objects exist when out of sight—are observed. The abilities of autistic children, 3 to 5 years of age, are compared with those of mentally retarded and normal children of comparable mental age. Object use in play natural settings, and experimental tasks is studied in relationship to the child's level of receptive and expressive language.

The Schizophrenic and His Family: Violent Subgroups
MH 00175; $40,986

Singer, Margaret T.
University of California
San Francisco, CA

The investigator is extending her studies of schizophrenia in three general areas. In one area of research, attention is paid to identification of those familial factors which may operate to produce the syndrome defined as schizophrenia and contribute to the development and/or maintenance of passive or violent behavior. Attempts are made to identify the characteristics which differentiate paranoid from nonparanoid delusional thinking in schizophrenics and their families; to determine the amount, types, and effects of violent behavior in these families; and to compare paranoid and nonparanoid patients and their families in the area of cognitive styles and behavioral controls. Data already collected on schizophrenic patients and their families are reanalyzed to differentiate the aggressive from the violent subgroups. Several populations, which have exhibited different levels of hostile behavior, are compared. The goal is to develop a method of early identification of potentially dangerous persons and plan appropriate interventions. In a second area of research, studies are made of the effects on young children of a borderline schizophrenic parent in the home. In a third area of research, studies are made of the effectiveness of various interventive therapies on paranoid schizophrenia.

Linguistic Models and Schizophrenic Communication
MH 31360; $59,011

Singer, Margaret T.
The Wright Institute
Berkeley, CA

The language of schizophrenics is studied. The research is based on a typology, developed by Margaret Singer, which classifies schizophrenic communication problems into five groups: commitment problems, referent problems, disruptions, language anomalies, and contradictions. Three experiments are aimed at describing schizophrenic linguistic phenomena in such a manner as to aid in the formulation of a new or revised typology. The practical application of this redesigned typology is assessed in relation to the early detection of schizophrenia and in relation to the differential diagnosis of paranoid versus nonparanoid and violent versus nonviolent schizophrenics.

Drugs and Electroconvulsive Therapy in the Treatment of Schizophrenia
MH 27519; $56,812

Small, Joyce G.
Larue D. Carter Memorial Hospital
Indianapolis, IN

The hypothesis that electroconvulsive therapy (ECT) in combination with a neuroleptic drug is more efficacious than the drug alone in the treatment of newly admitted, acutely psychotic schizophrenics is tested. Patients are randomly assigned to different treatment methods: 50 receive thiothixene alone; 50 receive the drug plus ECT; 30 receive unilateral ECT plus placebo; and 15 receive placebo alone. Social adjustment ratings are obtained every 3 months after discharge.

Psychiatric Disorders: Methodology for Family Studies
MH 33617; $42,437

Spence, Mary A.
University of California
Los Angeles, CA

Genetic methodology is developed for family studies in behavior disorders, such as bipolar affective disorder and schizophrenia. The methods are specifically designed to detect the effect of single genes in the presence of four known complicating factors: reduced penetrance, assortative mating, association, and ascertainment bias. The methods are applied to a data set of approximately 150 families of manic-depressive individuals, and results are compared with results obtained through standard analyses.

Attention, Thought Disorder and Drug Action in Schizophrenia
MH 32220; $124,582

Spohn, Herbert E.
Menninger Foundation
Topeka, KS

The effects of antipsychotic drugs on cognitive dysfunctions in schizophrenia are examined. Hypotheses pertaining to the specific nature of information processing dysfunction and attentional defenses in chronic schizophrenics are tested. The effects of antipsychotic drugs on cognitive dysfunction and nonvoluntary attention disorders—as measured by pursuit eye movements—are investigated. The viability of a behavioral/psychophysiological—selective attention dysfunction/skin conductance reactivity—model of therapeutic drug action is tested. Interrelationships among measures of cognitive dysfunction, attention dysfunction, and generalized deficit functioning are explored. The research design involves approximately 135 chronic schizophrenic subjects who are randomly assigned to either an abrupt medication withdrawal group or a medication continuation control group. The research includes a systematic assessment for withdrawal-emergent tardive dyskinesia.

Attention Dysfunction in Schizophrenia
MH 32355; $61,242

Spring, Bonnie J.
Harvard College
Cambridge, MA

The first research goal is to determine if either a dysfunction in selective attention or a dysfunction in vigilance attention is specific to schizophrenia. The second research goal is to test the relatives of schizophrenic individuals in order to ascertain if either of these dysfunctions is a marker of a predisposition to schizophrenia. Selective attention is measured in a dichotic listening task, in which the subject, who wears earphones, is presented with two simultaneous messages, one to each ear. Vigilance is measured by reaction time. Focus is on crossover reaction time, a faster reaction time for irregular preparatory intervals than regular preparatory intervals. Subjects are normal individuals; schizophrenic, bipolar depressed, and nonpsychotic patients; and relatives of patients.

Memory as Affected by Aging, Disease, and Electroconvulsive Therapy (ECT)
MH 24600; $105,732

Squire, Larry R.
University of California
La Jolla, CA

Memory dysfunction is studied in humans as a function of aging, in neurological disorders, and as a side effect of electroconvulsive therapy (ECT). A questionnaire is constructed based on randomly selected news events over the past 40 years. This questionnaire is presented to a homogeneous sample of elderly people to see if an objective forgetting curve for remote events can be established. A homogeneous sample of 50-, 60-, 70-, and 80-year-old amnesic inpatients is questioned in a second study to determine if loss of memory is general, not time-related, or time-related. The same questions and a test of intelligence are administered to the chronically amnesic individuals. Patients who undergo a series of ECT are interviewed, and various biographical data are collected from different periods of the patient's life. These patients are given the Zung Self-Rating Scale for Depression and the verbal scale of an intelligence test to determine if impaired performance is attributable to confusion. Other studies parallel current animal studies in the field of memory dysfunction and test a variety of features of memory loss immediately following ECT episodes.

In 1979, the amnesic syndrome is studied in ECT patients and patients with Korsakoff's psychosis. The amnesic syndrome is compared to the memory impairment associated with depression and normal aging in subjects 50 to 80 years old. The possible memory dysfunction associated with regimens of psychotropic drugs is assessed, and specific hypotheses concerning the pharmacology of memory in man are tested. Drugs utilized include lithium, phenothiazine tranquilizers, cholinergic compounds, and marijuana. The extent and duration of memory dysfunction associated with ECT is also examined. Parameters of electroconvulsive shock are studied in animals.

Effects of Psychotherapy in Schizophrenia
MH 25246; $362,749

Stanton, Alfred H.
McLean Hospital
Belmont, MA

An intensive psychotherapy program for hospitalized schizophrenic patients is compared with that of general hospital psychiatric treatment. Primarily, the researcher is attempting to determine the most successful treatment methods and the characteristics of patients most suitable for this type of therapy. He also hopes to contribute toward the definition of the traits of a therapeutically effective clinician. A number of baseline measures are administered to subjects upon admission to the study; many of these tests are repeated through the 3 years of treatment, with a followup after discharge for a longer period. The relation of outcome to experience, frequency of treatment, degree of treatment involvement, demographic background characteristics of the patient, the factors—such as cognitive, emotional, and role-performance—responding to both types of treatment, and other characteristics are examined periodically.

Beginning in 1978, primary efforts were aimed at maintaining uniformity of conditions for this collaborative comparison of treatment of hospitalized schizophrenia patients by intensive psychoanalytic therapy or treatment as usual. The collaborative study is P01 MH 026183.

Prospective Study of Tardive Dyskinesia Development
MH 32369; $103,203

Struve, Frederick A.
Long Island Jewish-Hillside
Medical Center
New Hyde Park, NY

A longitudinal prospective followup investigation of the parameters affecting the development of dyskinesia symptomatology and clinically diagnosed tardive dyskinesia is performed utilizing a large number of subjects exposed to neuroleptic medication. The objective is to study the longitudinal development of neuroleptically induced dyskinesias and to assess empirically the relationship of tardive dyskinesia to a number of risk variables, such as age, medication exposure, and a distinctive electroencephalogram (EEG) wave form. Subjects are psychiatric patients with varying diagnoses.

Auditory Discrimination in Infantile Autism
MH 31679; $57,285

Tanguay, Peter E.
University of California
Los Angeles, CA

Possible electrophysiological differences in auditory discrimination between normal, retarded (Down's syndrome), and autistic children are studied. Data gathered on reprocessed, filtered, single evoked response to stimuli consisting of time-matched and pitch-matched words and musical chords are analyzed. Subjects are autistic children, ages 2 to 12.

Neuropsychopharmacological Studies of Attention
MH 00016; $9,477

Tecce, Joseph J.
Tufts University
Boston, MA

Research in the field of attention is continuing through the use of scalp-recorded contingent negative variation (CNV) and behavioral measures to investigate the interaction of drugs and attention disorders in schizophrenic patients and individuals without diagnosed disorder. During the period of support, specific tasks are to be accomplished: the use of CNV and attention performance during distraction to measure therapeutic response of schizophrenics to phenothiazines; a similar investigation on attention behavior of anxiety neurotics; an investigation of antagonistic psychotropic drugs—amphetamine and chlorpromazine—as they influence CNV's in normal subjects; further investigation of the usefulness of CNV shape as a predictor of response to drugs by normal and patient groups; extension of investigations of topographical differentiation of CNV over various areas of the brain; and examination of relationships between electroencephalogram (EEG) and CNV in different brain areas as a function of attention states related to distraction and drugs.

Search for Genetic Markers in Psychoses
MH 29686; $29,276

Turner, William J.
State Department of Mental Hygiene, Long Island Research Institute
Stony Brook, NY

Human leukocyte antigen (HLA) typing is performed utilizing patients with schizophrenia and affective psychoses, their first degree relatives, and control subjects. The aim is to study the possibility of a genetic marker on Chromosome 6 for schizophrenia and bipolar affective disorders, which may be associated with the human leukocyte antigen locus.

The Impact of Mental Illness on Patients' Families
MH 34325; $10,856

Vine, Phyllis S.
Sarah Lawrence College
Bronxville, NY

The impact of a live-in, chronically mentally ill relative on the middle class family is studied. Previously collected interview data from parents, siblings, children, and spouses of individuals with major psychotic episodes are analyzed. The analysis focuses on: cyclical disruptions in family life due to multiple hospitalizations; frustrating attempts to get help; difficulties in reintegrating the patient into the family unit after discharge; feelings of shame, guilt, stigmatization, isolation, and uniqueness; and the exacerbation of self-reproach by the behaviors of others.

Platelet Monoamine Oxidase (MAO) in Chronic Schizophrenics
MH 31156; $64,649

Vogel, Wolfgang H.
Thomas Jefferson University
Philadelphia, PA

The kinetic properties of platelet monoamine oxidase in schizophrenic patients, in their relatives, and in control subjects are examined using various substrates, including biogenic amines, dimethyltryptamine, and 5-methoxytryptamine. The possible presence of an endogenous inhibitor of platelet monoamine oxidase in the plasma of some patients is also investigated by incubating platelet-free plasma of chronic schizophrenics with platelet monoamine oxidase of normal volunteers.

Effects of Lecithin in Tardive Dyskinesia
MH 34558; $97,505

Volavka, Jan V.
Rockland Research Institute
Orangeburg, NY

The therapeutic efficacy of lecithin in the treatment of tardive dyskinesia is examined in approximately 50 patients with the disorder. Lecithin tolerance, side effects, and duration of effects are explored. Physiological, social, and psychological differences between patients who respond to lecithin and those who do not are examined, and blood levels of lecithin and choline are correlated with clinical response.

Major Mental Illness: Genetic/Environment Relationships
MH 00299; $37,904

Wagener, Diane K.
University of Pittsburgh
Pittsburgh, PA

Family study methods are utilized to obtain data relevant to the heritability of the major psychiatric disorders. Serotonin uptake rates by platelets are studied in patients with unipolar and bipolar depression and in their relatives. Sleep electroencephalograms are studied in normal children, ages 6 to 17 years, and their parents. Attentional tests are given to family members of schizophrenic patients as part of a collaborative study of genetic/environmental interactions of vulnerabilities.

Evoked Potentials in Outpatient Schizophrenics
MH 32595; $62,462

Wagman, Althea M.
University of Maryland
Baltimore, MD

Visual and somatosensory evoked potentials are studied in outpatient schizophrenic individuals who are experiencing symptom remission. Patients receive either standard psychopharmacological therapy or drug-free psychosocial treatment. All patients are tested repeatedly throughout a 2-year period to determine whether evoked potential response variables serve as prognostic indicators of therapy outcome. Determining the effects of haloperidol on the evoked potentials of schizophrenic patients is among the specific aims of the research.

Regulation of Dopamine Neurons and Schizophrenia
MH 34424; $75,397

Wang, Rex Y.
Saint Louis University
Saint Louis, MO

The neurophysiology, regulation, functional characteristics, and afferent input of dopaminergic neurons in the rat midbrain ventral tegmental area are examined, for the possible role of these neurons in the actions of antipsychotic drugs and in the pathogenesis of schizophrenia.

Language Behavior in Autistic and Schizophrenic Children
MH 26805; $81,199

Waterhouse, Lynn H.
Trenton State College
Trenton, NJ

Language deficits and behavior in autistic, schizophrenic, and normal children 5 to 12 years old are studied and compared. Vocabulary, sentence repetition, spontaneous speech, and the behavioral context of speech are aspects investigated. Performance on generalization tasks for both language and cognition are measured. Subjects include 20 children diagnosed as autistic and 20 who are schizophrenic. Data are also collected on three control groups: children matched with the autistic and schizophrenic for mean length of utterance in spontaneous speech; performance scores on standard tests; and chronological age. The data gathered are used to explore the theoretical controversy of autism and childhood schizophrenia as single or separate syndromes. They also provide evidence relating to the question of their being the result of local brain damage or a general functional impairment. Data deal with the contention of their behavior as delayed/normal or bizarre. The negative, neutral, or positive response to input intensity for autistic children is measured by the data.

In 1976, the study is continued in order to chart linguistic, visual perception, and kinesic performance of 100 psychotic children, 6 to 15 years old, and approximately 200 normal controls matched in terms of chronological age or on a developmental linguistic measure—mean length of utterance. The study adds new data relevant to the semantic development of the disturbed children. Additional tests are included to determine whether any identifiable neurological syndrome is associated with schizophrenia or autism, and whether certain behaviors can be tied to certain neurological impairments.

In 1978, the investigator continues the exploration of visual perceptual skills and language skills in 72 of the psychotic children being studied. Greater emphasis, however, is placed on psychometric evaluation of the subjects.

Behavioral Study of Children of Schizophrenic Parents
MH 32667; $60,326

Watt, Norman F.
University of Denver
Denver, CO

A longitudinal investigation of the social and intellectual behavior of children known to be at high risk for the eventual manifestation of schizophrenia is made. The primary purpose is to procure teacher ratings of classroom behavior and objective data on scholastic performance, attendance, and conduct at school for children of one schizophrenic parent, children of two schizophrenic parents, children of psychiatrically-disordered—but not schizophrenic—parents, and children of normal parents. The age range of the children upon initial examination is 7 to 12 years, and followup behavioral assessment is made at 13 to 18 years of age. Approximately 20 percent of the sample is selected as behaviorally maladjusted, and consequently most vulnerable to subsequent emotional disorder.

Plenary Conference of the Risk Research Consortium
MH 33954; $19,487

Watt, Norman F.

University of Denver
Denver, CO

A conference on longitudinal research of children, adolescents, and adults at high risk for schizophrenia and related disorders was held. The international conference included a symposium on behavioral adjustment of children at risk, and a symposium on assessment and outcome. There are also four topical workshops to permit a specialized exchange of research interests dealing with infancy and preschool behavior, stress, social support and intervention, psychophysiological functions, and family relations.

Impact of Affectively Ill Parents on Their Children
MH 35114; $121,176

Weintraub, Sheldon
State University of New York
Stony Brook, NY

Approximately 377 children between the ages of 7 and 15 years, including 243 children with an affectively ill or schizophrenic parent, are studied. In addition, a supplementary sample of 82 adults, 18 to 21 years of age, are examined. These adults, previously assessed at school age, are also children of a mentally ill parent. A detailed picture of the characteristics of children with a parent diagnosed as unipolar depressed, bipolar, schizophrenic, or normal is obtained. Child characteristics are related to parental diagnosis and environmental variables in the home and school. Particularly vulnerable and invulnerable children are characterized. The ways in which the family unit are affected by and cope with the stresses of psychiatric disorder and hospitalization are assessed. Precursors specific to the development of depression and schizophrenia are identified.

Effects of Psychopharmacologic Agents on Behavior
MH 11752; $92,973

Weiss, Bernard
University of Rochester
Rochester, NY

Relations among the dosage and duration of treatment with psychotropic or toxic agents, neurochemical reactions, and behaviors are measured in this study. Animals, including primates, serve as subjects. The strength of environmental perceptual stimuli, other environmental variables, and previous drug exposure are correlated with behavioral response to chronic drugs and toxins. Brain catecholamines and neurohistological changes are also measured. Computers are used extensively in programming stimuli as well as in data analysis. The drugs involved include amphetamine, chlorpromazine, alcohol, methamphetamine, scopolamine, haloperidol, physostigmine, phencyclidine, heavy metals, and marijuana. In addition, the investigator is examining the effects of drug treatment on work and thinking in college students.

Gene Linkage and Familial Behavioral Characteristics
MH 00124; $35,285

Weitkamp, Lowell R.
University of Rochester
Rochester, NY

Attempts are made to demonstrate the existence of a major gene determining schizophrenia or a depressive psychosis by linking the postulated gene to a polymorphic marker gene such as one of the blood groups. First, searches are made for large pedigrees in which a functional psychosis appears to be segregating as an autosomal dominant gene. Then, each available family member is typed at each of 35 or more polymorphic marker loci. Linkage to a given marker is evaluated statistically over a range of recombination fractions by a likelihood ratio test.

Untreated Psychiatric Disorder in a Peasant Society
MH 34322; $16,813

Westermeyer, Joseph J.
University of Minnesota
Minneapolis, MN

An assessment is made of the social functioning and psychopathology of individuals labeled as *baa* (severely mentally unbalanced) in Laos where no modern or Western psychiatric services are available. Since such services are not available in Laos, and since the *baa* condition is not viewed as a medical one, there is the opportunity to dissociate mental illness from treatment and institutionalization factors. Data previously collected in Laos are based on common standardized tests, clinical interviews, and interviews with family and village acquaintances. Findings are compared with data on psychotic patients in the United States.

Neuroleptic Drugs and Dopamine Metabolism
MH 21638; $85,233

Wilk, Sherwin
Mount Sinai School of Medicine
New York, NY

The cerebral metabolism of dopamine and norepinephrine is investigated in various brain regions, ages, and species, and the effects of neuroleptic drugs on these metabolic patterns are examined. Measurement of catecholamine metabolite levels in the cerebral spinal fluid of patients with schizophrenic or affective disorders are made before, during, and after drug therapy. A model for predicting efficacy of antipsychotic drugs is developed, based on dopamine metabolite levels in rat brain. The relationship between manipulation of γ-aminobutyric acid levels and dopamine metabolism is also examined.

Neuropathologic Analyses of Neuropsychiatric Disorders
MH 34079; $106,899

Williams, Roger S.
McLean Hospital
Belmont, MA

Computer-assisted quantitative histological techniques are developed to identify structural abnormalities in the single neuron. The sensitivity of this technique is tested in postmortem cortical tissue from patients with Huntington's disease. Various areas of postmortem cortex tissue from schizophrenic and autistic patients are subsequently examined. Animal studies in rodents, including strains with congenital cortical malformations, are also conducted.

Children and Families Vulnerable to Mental Disorders
MH 22836; $409,881

Wynne, Lyman C.
University of Rochester
Rochester, NY

Children of mothers with schizophrenia or other psychiatric disorders are studied. These children, Caucasians between the ages of 1 and 10, are each followed for 3 years to examine developmental patterns of cognitive, emotional, social, and psychophysiological functioning. The objective is to identify early indicators of psychiatric illness among these high-risk children and relate their attributes to characteristics of their parents. The study focuses with equal intensity on the large majority of children in this sample who are unlikely to develop a mental illness. Personal and familial factors are investigated that will help most of the subjects to develop normally, despite the possible genetic loading or predisposition to illness and despite the presence and influence of a schizophrenic mother in the family. The studies are carried out in the home, school, and clinic, and they involve psychiatric interviews, observation, and testing.

In studies beginning in 1978, emphasis continues to be on interpersonal and environmental factors in the lives of the individuals longitudinally under study. Project titles and investigators include:

Strauss, J.: Parent Diagnostic Assessment.

Ritzler, B.: Parent Psychological Test Assessment.

Romano, J.: Family Assessment: Parenting and the Caretaking Process.

Baldwin, A.: Family Free Play Interaction.

Baldwin, A.: Child Assessment: Child's Developmental History.

Jones, F.: Child Assessment: Current Social Competence.

Fisher, L.: Child Assessment: School Competence.

Space, L.: Child Assessment: Intellectual Testing.

Chandler, M.: Standardized Child Personality Assessment: Piagetian Developmental Studies.

Fisher, L.: Child Personality: Attention Measures. Child Personality: Censure/Praise Measures.

Baldwin, A.: Child Clinical: Psychological Tests.

Munson, S.: Child Clinical: Psychiatric.

In 1981, data for the 3-year followup have been collected. Parental diagnoses include schizophrenic psychosis, schizoaffective disorder, bipolar affective psychosis, unipolar psychotic depression, nonpsychotic depression, and severe personality disorders. Data analysis emphasizes the child, parent, and family areas, and the relationships among these areas. Child clinical assessment focuses on global assessment, integration of various types of child data, and diagnosis. Parental assessment includes detailed information about social and work competence, as well as diagnosis. There are three domains of family variables: cognitive/attentional (especially communication deviance), relational/structural (including power and dominance), and affective (warmth).

World Health Organization/National Institute of Mental Health Study of Determinants of Mental Disorders
MH 30322; $75,798

Wynne, Lyman C.
University of Rochester
Rochester, NY

A United States Field Research

Center is reestablished as a collaborating unit in an ongoing project of the National Institute of Mental Health and the World Health Organization (WHO) which is studying various determinants associated with the course and outcome of major mental disorders, especially schizophrenia. There are three areas of emphasis: a study of patients and their families with the standard methods and instruments which are used in WHO field centers in Hawaii and Japan; development of family assessment methods for cross-cultural use; and a sociocultural study of Monroe County, the catchment area.

Chlorpromazine-Induced Immunopathy
MH 33684; $89,200

Zucker, Stanley
Veterans Administration Medical Center
Northport, NY

Immune abnormalities correlated with duration and dose of chlorpromazine treatment are examined in newly diagnosed schizophrenics beginning chlorpromazine treatment, and in schizophrenics chronically treated with chlorpromazine and identified as having chlorpromazine-related immunopathies. Comparisons in immune abnormalities are made over a 3-year period in patients receiving chlorpromazine or haloperidol, and the class of immunoglobulins involved in these abnormalities is investigated.

Division of Manpower and Training Programs

Training for Church-Based Aftercare Programs
MH 16521; $38,820

Anderson, Robert G.
Yale New Haven Hospital
New Haven, CT

The goal of this program is to promote, identify, train, and consult with leaders in religious and mental health agencies to facilitate the establishment of collaborative, community-based aftercare programs for the chronically disabled mental patient. The training and consultation is divided into three stages. Stage one focuses on developing agreements between religious and mental health organizations to explore the establishment of a collaborative aftercare program. The aim is to generate cooperative work units which can be trained to organize appropriate aftercare programs. Stage two provides intensive training sessions focused on interdisciplinary/collaborative strategies. Sessions are designed to provide a thorough understanding of community-based aftercare. Stage three provides followup field consultation and training to support the work units.

Chronic Care, Advanced Psychiatric Nursing
MH 16168; $117,650

Banchik, Doris
Yale University
New Haven, CT

A chronic care concentration in adult psychiatric mental health nursing is developed and implemented. Nursing students are prepared in a 2-year master's program to serve in inpatient, outpatient, community liaison, and rehabilitation assignments in public mental health facilities. There is an emphasis on community mental health, with a specific focus on the care of the chronically ill.

Training Psychiatrists for Public Mental Health Service
MH 16202; $76,810

Bernal, Victor J.
Puerto Rico Institute of Psychiatry
San Juan, PR

A special residency program provides training in public psychiatry to Puerto Rican physicians. The training is relevant to serving the population of underserved or unserved areas of Puerto Rico and caring for the chronic or severely ill mental patients.

Mental Health Services Manpower Systems Development Program
MH 16462; $143,726

Biskin, Donald
State Department of Mental Health and Mental Retardation
Richmond, VA

A State mental health services manpower planning and policy development capability is established to improve the allocation, distribution, utilization, and productivity of mental health professionals and paraprofessionals in Virginia. Staffing requirements for appropriately meeting the service needs of the chronically and severely mentally ill, and the mentally ill/behaviorally disturbed child or adolescent receive priority consideration. Recruitment, retention, and appropriate distribution of qualified psychiatrists and qualified minorities within the State's mental health system are also assessed.

Competency-Based Training for Treatment of Autism
MH 15614; $71,997

Blackwell, Lois J.
Juvenile Center for Autistic Children
Saint Louis, MO

A core unit consisting of an administrator, a professional, and a parent or a second professional is trained in implementing a program that is effective in teaching autistic children. Trainees are from the same facility and are expected to return to their local program and replicate the Judevine system. The parent must have an autistic child who comes with the parent during the training, and who subsequently is a student in the home program. The systematic training of the core groups in the Judevine system of competency-based learning/treatment also provides the skills needed for training trainers at the home location. A modular program is designed to move children in a sequential developmental manner regardless of the severity of their problem behavior. Training procedures are based on operant learning principles which build desirable functional classroom behaviors while diminishing inappropriate behaviors.

Graduate Program in Advanced Psychiatric Nursing
MH 16213; $105,806

Blenner, Janet L.
University of San Diego
San Diego, CA

Training is provided in psychiatric nursing at the Master's level. The service is provided to the chronically ill client who has spent a lifetime of institutionalization, sporadically reentering the community, but is functioning poorly and unable to cope with the activities of daily life. Emphasis is on aiding the client in learning decisionmaking, and family therapy to help the family reintegrate the client into the family as well as the community.

Mental Health Service Delivery Research and Evaluation
MH 14609; $96,751

Callaway, Enoch
University of California
San Francisco, CA

This program provides postdoctoral fellowships for clinical research on mental disease and maladaptive behavior. With assistance and supervision from a multidisciplinary faculty, fellows have the opportunity to plan and carry out research designed to develop new methods of prevention, diagnosis, and/or treatment; and evaluate preventive, diagnostic, and/or therapeutic procedures. These studies may be carried out in community health care delivery systems as well as in special research environments. A training committee assigns each fellow to a principal preceptor and works with the preceptor to establish a program tailored to the needs of the particular fellow, including laboratory research, university classes, community resources and directed reading. The programs include psychotherapy evaluation study; health psychology program; community service and research programs; drug dependence treatment research group; studies in depressive and suicidal states; emotional disturbances of the elderly; facial behavior in diagnosis and treatment; neurology, sound, speech, and language studies; studies of lateral specialization; clinical psychopharmacology; and studies of the diagnosis and treatment of the major psychoses.

Psychiatry Nursing of Chronically Ill in Public Mental Health Systems
MH 16199; $83,537

Chisholm, Margery M.
Boston University
Boston, MA

Graduate nurses are trained at the Master's level for positions of leadership while focusing on the clinical care of the chronically mentally ill patient. Emphasis is on the development of psychiatric primary care skills within a community systems approach, utilizing public mental health service facilities. The program is unique in teaching physical and mental health assessment skills.

Project Aspire
MH 15451; $109,414

Crawford, Priscilla
Indiana Department of Mental Health
Indianapolis, IN

The goals of this project are to develop more effective procedures for providing services to mentally disabled citizens, demonstrate methods of service delivery, train personnel for the delivery of services, and to evaluate the quality of services delivered. Project ASPIRE (Attendant Support in Programming for Individual Residents) is intended to: fulfill the continuing education needs, provide the training to meet deinstitutionalization needs, and establish career advancement opportunities for paraprofessionals in mental health. Two sets of individualized transportable training packages are developed for paraprofessionals in mental health. The first set targets generic assessment and programming techniques for implementing individual program plans for mentally disabled clients. The second set includes subsets specifically targeting skills for servicing the particular mentally disabled populations served by the Indiana Department of Mental Health.

Research Training—Biological Sciences
MH 14620; $45,904

Crowe, Raymond R.
University of Iowa
Iowa City, IA

This is a 1- to 2-year postdoctoral fellowship program in psychiatric genetics. The objective is to train fellows in the principles of genetics, the literature in psychiatric genetics, and research methods in psychiatric genetics. The research training centers around the major psychiatric syndromes, including schizophrenia, affective disorder, alcoholism, and antisocial personality. The program accepts any candidate with a doctoral degree and some prior training in the mental health field.

Home Care Training for Caretakers and Mental Health Staff
MH 15056; $86,400

Egan, Kathleen L.
Horizon House Institute for Research and Development, Inc.
Philadelphia, PA

Training is provided for approximately 250 boarding home proprietors serving persons disabled by mental illness and long-term institutionalization. The project has three major goals. The first is to facilitate the establishment of residential environments which promote the well-being of deinstitutionalized persons. The second is to provide a training model which increases the proprietors' skills and competencies, while at the same time increasing their status in the delivery system and recognizing their caregiving function as paraprofessionals. The third goal is to improve long-term working relationships between the proprietors and community mental health agencies who need to share the responsibility for client care and support. Training is provided in brief sessions over a 15-week period.

Beginning in 1979, continuing education is provided to boarding home proprietors who have completed the initial course, and inservice training is provided to staff of mental health centers to promote better coordination between mental health center staff and boarding home proprietors.

Psychiatric/Mental Health Nursing
MH 16173; $104,488

Forbes, Beverly S.
Indiana University Foundation
Indianapolis, IN

This program prepares clinical specialists in psychiatric-mental health nursing for a variety of roles in working with the chronic and aging mentally ill in Indiana. The program emphasizes the development of skills in trainees for evaluating psychotherapeutic models from psychiatry, psychology, and social sciences as well as nursing; the establishment of linkages between the graduate nursing program and the statewide level facilitating service delivery; and the recruitment of students being placed in state public mental health sector after training.

Targeted Education in Investigative Psychiatry
MH 07336; $81,000

Freedman, Nobert
Downstate Medical Center
Brooklyn, NY

This program is a research training program in psychiatry. The basic theory and techniques for investigation in psychiatry and in a number of related fields such as psychology, neurophysiology, biochemistry, and sociology are studied. Upon entering the program, trainees begin research work through participating in an ongoing research project. Later they develop an investigation of their own.

In 1980, medical students, residents, and postresidency fellows in psychiatry are offered four areas of research subspecialization. These areas are: biological psychiatry in the study of chronic mental illness; developmental (infant and child) studies and preventive strategies; evaluation research and the study of community support systems; and communicative processes in the treatment process.

Mental Health Nursing Graduate Program
MH 16207; $92,140

Garner, Grayce S.
University of Rhode Island
Kingston, RI

A graduate program at the Master's level is offered in mental health nursing. Direct practice is provided with agencies and organizations within the public mental health delivery systems which serve severely impaired and mentally ill clients, including deinstitutionalized patients. Training is provided in the multidisciplinary approach to treatment in serving the needs of adolescents, adults, and the elderly in relation to their families, groups (organizations), and communities.

Psychiatry: Special Initiative
MH 16182; $59,400

Ginsberg, George
New York University
New York, NY

Psychiatric residents in their third and fourth years receive training designed to encourage them to practice in public mental health facilities serving the severely mentally disturbed. The target populations include delinquent and psychotic adolescents, mentally disturbed prisoners, the mentally disturbed aged, and the chronically psychosocially disabled. A significant proportion of the target population are members of black, Hispanic, or other minority groups. The program is based on a core curriculum with a minimum 6-month commitment providing an intensive exposure to the chronic patient population in the urban hospital, as well as the urban community.

Psychological Research on Schizophrenic Conditions
MH 14584; $40,591

Goldstein, Michael J.
University of California
Los Angeles, CA

This predoctoral and postdoctoral training program prepares students for research careers in the study of schizophrenia, especially possible familial and developmental precursors of schizophrenia. It draws its predoctoral students from the psychology department's ongoing predoctoral psychology training program. Its postdoctoral students are psychologists and psychiatrists with strong research interests in schizophrenia. A variety of relevant courses and seminars already offered in the department constitute the formal academic aspects of the program, and research training takes place in the ongoing projects of principal investigators associated with the program. Adjunct help for the training program is available through affiliated research projects located in the medical school and at the adjacent Veterans Administration Hospital. These projects are concerned with training in the evaluation of diagnostic methods and intervention programs.

In 1979, all trainees have a doctoral degree.

Training Mental Health Professionals for Chronic Care
MH 16178; $64,544

Gudeman, Jon E.
Harvard Medical School
Boston, MA

Advanced residents in psychiatry are trained in the care of the chronically mentally ill patient in the community. In addition, training in the care of the chronic patient is provided to other psychiatric residents and mental health workers in other disciplines.

Schizophrenia: Family Styles and Patient Outcome
MH 08311; $18,486

Heinrichs, Douglas
University of Maryland
Baltimore, MD

Patterns of interaction are studied in families of schizophrenic outpatients. The research emphasis is on two variables: communication deviance and expressed emotion. Changes in communication deviance and expressed emotionality are studied over time, and measures taken during relapse and remission periods are compared.

Adaptive Resources of High-Risk Adolescents
MH 07787; $19,603

Hirsch, Barton J.
Stanford University
Stanford, CA

The modifying effects of coping abilities and environmental supports of school and family are studied in adolescents who are experiencing stress, because they have either a schizophrenic parent or an alcoholic parent.

Nursing: Psychiatric Care of Chronically Ill
MH 16180; $71,492

Ipema, Donna K.
University of Illinois
Chicago, IL

The primary objective of this program is to train psychiatric nurses at the Master's level to practice with the chronically and/or severely mentally ill patient. Other objectives are to provide training relevant to aged and rural populations. Basic theory courses of the current community mental health nursing curriculum are retained, and material relevant to the severely ill, the aged, and rural population groups is added. The communities served by the program have many black and native American minority group members.

Experimental Psychopathology and Brain Dysfunction
MH 07920; $19,040

Josiassen, Richard C.
Temple University
Philadelphia, PA

Electrophysiological techniques are utilized to study hypothesized brain dysfunction in patients diagnosed as having schizotypal personality disorder, because they exhibit disturbances of cognition, perception, communication, and behavior which are episodic or never severe enough to meet the criteria of schizophrenia. Evoked potentials are recorded in individuals with schizotypal personality disorder, latent schizophrenia, and chronic schizophrenia.

Psychiatric Services in Public Mental Health Settings
MH 16161; $73,086

Kaplan, Seymour R.
Yeshiva University
Bronx, NY

Specialized training experiences are provided for third and fourth year psychiatric residents. The training is concerned with public mental health services, and services for chronically mentally ill persons in public settings. The residents participate in didactic seminars and complete clinical assignments, usually in ambulatory treatment or community-based settings.

Metabolism and Pharmacology of Thioridazine
MH 07926; $20,546

Kilts, Clinton D.
University of North Carolina
Chapel Hill, NC

Changes in absorption, distribution, metabolism, excretion, and pharmacologic actions of thioridazine are examined in animals of different ages. Thioridazine metabolic patterns are compared in plasma and urine samples from children and from adult schizophrenic patients receiving this medication.

Community-Based Training Programs
MH 014761; $144,158

Kozloff, Martin A.
Boston University
Boston, MA

A community-based system is developed for providing behavioral training for persons in contact with children having a variety of mental health related problems (autistic, mentally retarded, learning-disabled, hyperactive). The system is based on the establishment of contingencies of reinforcement. It is intended for a number of groups: parents and siblings of such children, and junior and senior high school students and college students wishing to learn to work with such children. In addition, through the system, community members (administrators, teachers and parents) can learn to plan, implement, monitor, and evaluate their own training programs. Program evaluation is based on effects of the training program on trainees, changes in the behavior of the children, changes in the community's service delivery system, and costs of the community training program both to the project and to the community.

Operation Community Support, Hawaii
MH 13590; $66,991

Kurren, Oscar
University of Hawaii
Honolulu, HI

Master's level social work students are trained in community mental health in a program that focuses on comprehensive child mental health and problems of children in school. Mental health centers serve as the setting for the social work training. Field and class content are problem-centered with primary prevention as the focus of services. Pretests and post-tests measure changes in the students' behavior, knowledge, and attitudes. Changes in the mental health system and the university system are also considered in evaluating the project.

In 1980, the program prepares social workers in providing community support services to the chronically mentally ill in the multiethnic population of Hawaii. The objectives are: to develop a capacity for identifying adult populations who have severe and persistent mental or emotional disorders which limit their capacity to maintain primary aspects of daily living; to develop advocacy awareness of entitlements; to develop skill in the design, organization, and delivery of psychosocial rehabilitation services; and to become knowledgeable and skillful in the use of community supportive arrangements including mutual support systems and natural-helping networks. Ethnic minority students are recruited for training in community mental health service roles to serve diverse minority populations.

Nursing of the Chronically Mentally Disabled
MH 16209; $129,398

Lowery, Barbara J.
University of Pennsylvania
Philadelphia, PA

The program prepares a "generalist" clinician who can apply the nursing process within a systems theoretical framework, inclusive of individual, family, and community systems. Trainees work therapeutically with individuals in institutions, or in aftercare settings, and become actively involved in promoting the development of essential noninstitutional settings for care. Students develop skills in assisting families to give care in their homes. A specialist also provides contact or primary care with other agencies and services to provide respite, support, and other services to add quality to the lives of the chronic mentally disabled.

Psychiatric Nursing Graduate Education
MH 16181; $57,612

Lyss, Liny E.
University of Missouri
Columbia, MO

Psychiatric nurses are prepared at the Master's level for care of the chronic or severely ill patient in public mental health delivery systems. Emphasis is on rural needs in Missouri. The program focuses on health maintenance and self-care, and provides students with skills in working directly with the chronically ill, and with community and family support systems available.

Research Training, Social/Behavioral Sciences
MH 14246; $104,570

Mishler, Elliot G.
Harvard Medical School
Boston, MA

Advanced training through a combination of study and practice in ongoing research in a consortium of laboratories, appropriate courses, and interdisciplinary seminars is provided for postdoctoral fellows and psychiatrists. The consortium consists of four clinical training institutions: Massachusetts General Hospital/Lindemann Mental Health Center, Massachusetts Mental Health Center, McLean Hospital, and Cambridge Hospital. Training is in nine designated priority areas in mental health: alcoholism, drug abuse, child mental health, depression/suicide, schizophrenia, psychoactive drugs, minorities, evaluation, and mental health services management.

Training Program in Interpersonal Systems
MH 16165; $77,268

Mitsunaga, Betty K.
University of Washington
Seattle, WA

Interpersonal Systems Program is designed to prepare psychosocial nursing specialists at the Master's level for service to the chronically mentally disturbed population. Focus is on theories and research pertaining to chronic mental disability—etiology, the illness process, assessment, intervention techniques relevant to clients, and network interventions; consultation planning; and evaluation and field study in institutions and community agencies. Psychosocial nurses are also prepared to use innovative intervention modalities in their provision of care to the chronically mentally disabled population in multiple care settings; they are trained in alternative systems of mental health care modes of service delivery through research training and evaluation.

Psychiatric/Community Mental Health Nursing
MH 16175; $85,492

Newsome, Rebecca
Hampton Institute
Hampton, VA

This program develops, implements and evaluates a Master's Degree program in psychiatric/community mental health nursing. The chronic or severely impaired mentally ill in underserved and unserved public mental health service agencies participate in the program. Primary and secondary training sites selected are in the Tidewater area of Virginia.

Mental Health Services Manpower Systems Development Program
MH 16485; $149,577

O'Donnell, Francis G.
State Department of Mental Health and Corrections
Augusta, ME

Educational, training, and career development of skills/knowledge needs of workers who provide direct care to the mentally ill in Maine are assessed. Strategies to meet these needs are designed and implemented. Collaborative efforts with the Maine University System are concerned with comprehensive career ladders for the State's mental health institutes and community, curricula redesign, and career counseling. Needs of workers for the chronically mentally ill are emphasized.

Community Mode Coalitions: Patients/Ex-Patients/Staff
MH 16619; $82,234

Orlando, Norma J.
Elgin Mental Health Center
Elgin, IL

A community mode training model is designed to develop patient/ex-patient/staff coalitions and provide conditions for a basic change in the social/psychological arrangements in a mental health setting which not only produce chronic institutionalized patients and ex-patients, but demean and dehumanize staff as well. The Peer Leaders United Movement provides the basis for set-breaking, consciousness-raising training for patients, ex-patients, and frontline hospital staff, which is designed to enable the chronic mental patient to become his own change agent, divest himself of the loser mentality, and move toward an activist role in his own cause.

Public Sector Care of Inner-City Chronic Patients
MH 16428; $32,400

Randolph, Peter B.
Tufts University
Boston, MA

Psychiatric residents are trained to provide comprehensive and multidimensional treatment in the public sector for chronically mentally ill and disabled patients from an inner-city urban poverty area. Six areas of treatment are emphasized: individual, family, group, psychopharmacological, occupational and rehabilitative, and medical. Facilities of the Tufts/Bay Cove Community Mental Health Center are used for placement of residents to gain experience in a full range of State hospitals and community-based treatment facilities.

Graduate Psychiatric Nursing Specialist Training
MH 16169; $73,117

Rector, Cynthia A.
University of Alabama
Birmingham, AL

Psychiatric nurses are prepared at the Master's level to work with the chronic mentally ill in public mental health facilities. Nurses are trained to participate in planning, implementing, and evaluating treatment programs for the mentally ill in public mental health institutions in Alabama.

Community Social Work With the Chronically Mentally Ill
MH 15967; $81,922

Ross, Bernard
Portland State University
Portland, OR

Social workers with a Master's Degree in Social Work are instructed in planning, management, and direct service skills to respond to the service needs of chronically mentally ill persons who are being returned to the community. Organizing principles for the training program are the concepts of continuity and continuum of care and the examination of various service delivery programs and research findings which affect the care of this underserved population.

Research Training in Depression and Schizophrenia
MH 15144; $125,981

Sachar, Edward J.
Columbia University
New York, NY

Postdoctoral research training in the areas of depression and schizophrenia is offered as a 2-year fellowship program. It is designed to train psychiatrists and some psychologists for research careers in the study of affective disorders and schizophrenia. Curriculum contains courses on concepts of affective disorders and schizophrenia, statistical methods, psychobiology workshops, advanced scientific design and data analysis, electives chosen to meet specific needs, and departmental grand rounds with invited speakers.

Socialization and Mental Illness in Irish-Americans
MH 07210; $282

Scheper-Hughes, Nancy M.
Boston College
Chestnut Hill, MA

The relationship between socialization, family dynamics, and mental disorders is studied. The hypothesis tested is that a prevalent Irish stereotype of the good mother bears a striking resemblance to that described in the psychoanalytic literature as the schizophrenogenic mother. Subjects are 15 working class Irish-American families with a current history of mental illness in a postadolescent son or daughter, and a control sample of Irish-American families without incidence of psychopathology. Data are gathered on childrearing practices, the emotional tone of family interactions, and the development of schizophrenia in youth.

Psychiatric Residency Community and Forensic Emphasis
MH 16187; $80,356

Schwartz, Stuart R.
University of California
San Francisco, CA

Training for psychiatric residents is designed to provide effective work with chronic, seriously disabled patients in public settings. Special attention is given to problems of the inner city and forensic psychiatry. Another emphasis is on consultation/liaison skills, both within a hospital and with primary care physicians in general health centers. The residency involves an alliance between the University of California, the community mental health services of San Francisco, and San Francisco General Hospital.

Psychiatry, Community Mental Health
MH 16193; $75,600

Shore, James H.
University of Oregon
Portland, OR

Psychiatric residents are trained in the care, management, assessment, and rehabilitation of the chronically mentally ill patient in public settings, including State hospitals and mental health clinics. Residents in psychiatry are encouraged to develop a focus in working with a wide variety of service and community support systems for serving special underserved populations, either in hospitals or returning to the community.

Mental Health Clinical Practitioner Training Program
MH 14949; $112,673

Siegel, Martha A.
California State University
Long Beach, CA

Nurses are trained at the master's level to provide primary and preventive care in mental health settings in the community. Target populations include children and adults with chronic mental illness or developmental disabilities, who have been deinstitutionalized. This program is an integral part of the graduate program in nursing now offered at the Long Beach campus and the University of California at Irvine. Evaluation of the program includes an analysis of patterns of utilization of graduates as mental health clinical practitioners, and the impact of the role in reducing institutionalization of clients.

Special Initiative: Train Psychiatrist in Public Mental Health Service Facilities
MH 16200; $48,600

Snelson, D. Mark
Indiana University Foundation
Indianapolis, IN

Psychiatric residents in their fourth year of training, who have agreed to work at least 1 year after residency in a public psychiatric setting, receive training relevant to community mental health centers and State hospitals. Under supervision, the trainees assume direct care for a cohort of chronically mentally ill patients. A feature of the program is visits to the trainee's future job site and discussions of the particular problems at that site.

Training Psychiatry Residents: Community Service
MH 16185; $48,565

Stein, Leonard I.
University of Wisconsin
Madison, WI

The major educational objective of the Training Community Living Program is to prepare the psychiatric residents for different public sector careers. Focus is primarily on teaching skills for community treatment of the chronic psychiatric patient. Training takes place within the context of the community support system model. The resident learns to operate various elements of the system which include: being an ongoing consultant to community organizations in this system; working with chronic patients over an extended period of time; and consulting with rural mental health centers and with the University of Wisconsin Family Practice Clinic.

Residency Training: Care of Chronic Mental Illness
MH 07783; $72,242

Stein, Marvin
Mount Sinai School of Medicine
New York, NY

This program is providing psychiatric residency training for physicians to become psychiatrists. It offers training in the biological, psychological, psychiatric, and social approaches to the understanding, treatment, and prevention of mental and emotional illness. Lecture courses and demonstrations are given throughout the 3 years. The first year of training is in inpatient service; the second year emphasizes ambulatory care for adults, children, and adolescents; and the third year involves individual programs to afford the development of a variety of career choices, including clinical practice, academic careers, research, and community psychiatry.

In 1980, the overall objective of this program, which takes 4 years to complete, is to train physicians in the basic aspects of psychiatry. A major objective within the framework of training clinically competent psychiatrists is an emphasis on the training of psychiatrists in the care of the long-term patient with mental illness.

Interdisciplinary Research in Childhood Psychosis
MH 16381; $82,972

Tanguay, Peter E.
University of California
Los Angeles, CA

Postdoctoral students receive training designed to prepare them to carry out clinical research on the etiology, prevention, and treatment of psychotic conditions in infancy and childhood. The research training, which takes 2 years to complete, is provided within an interdisciplinary setting. Trainees have degrees in psychology, nursing, social work, child psychiatry, child neurology, or other disciplines.

Continuing Education in the Service of Chronic Psychiatric Patients
MH 15639; $91,800

Wolkon, George H.
University of Southern California
Los Angeles, CA

A continuing education program is conducted to: train mental health professionals in the private and public sectors as consultants to community care facilities in Los Angeles County in order to facilitate deinstitutionalization of psychiatric patients; train personnel of the State licensing bureau in the application of resocialization theories to State regulations, and in the use of resources to improve quality of care in community care facilities; train members of existing Citizen Advisory Groups which are concerned with the reintegration of psychiatric patients into community life; attempt to organize a coordinated comprehensive, integrated system for community care for the deinstitutionalized mental patient by means of continuing education; and evaluate the effectiveness of the training programs for the three target groups in terms of attitudes, beliefs, and skills of the trainees as well as benefits to individual clients, community care facilities, and organizations for service delivery.

Preparing Psychiatrists for Public Service Practice
MH 16201; $36,003

Woods, Sherwyn
University of Southern California
Los Angeles, CA

Third and fourth year psychiatric residents are provided with experiences in public psychiatric settings. Intensive training with traditionally underserved patients with chronic, long-term psychiatric illness is offered. The use of alternatives to hospital treatment for psychiatric patients is emphasized. The educational setting, a massive medical center complex, serves a majority of indigent patients from minority backgrounds of all types. One of the training sites is the El Centro Community Mental Health Center, located in the primarily Mexican-American section of East Los Angeles.

Division of Mental Health Service Programs

Strategy Development Project, Statewide Community Support System (CSS)
278-77-0107; $232,047

Alabama, State of
Montgomery, AL

This project develops a strategy for a statewide Community Support System (CSS). On the State level, this involves establishment of an organizational unit responsible for facilitating development and improvement of a CSS; promotion of a broad-based constituency within the State; completion of an assessment of CSS needs and resources within the State; an analysis of future manpower development, technical assistance, and training needs; and preparation of an interagency State CSS strategy. On the national level this involves: demonstration of methods by which a State mental health agency can provide leadership in mobilizing efforts toward CSSs; development of methods and materials for dissemination to other States attempting to improve CSSs; collection of baseline data on quality, availability, coordination, costs, and funding sources for CSS components at the beginning of the planning process; documentation of specific achievements, spinoffs, and problems encountered in the strategy development process; and clarification of resource requirements for CSSs, identification of obstacles within existing Federal, State, and local legislation and policies; and development of methods to overcome such obstacles.

Beginning in 1979, a State CSS Action Plan is prepared, completed, initiated, and evaluated. Also, a management system which integrates both programmatic and administrative elements into the process of monitoring is developed.

Determination of Environmental and Individual Contribution to Mental Disability
278-80-00014; $46,291

AMRON Management Consultants, Inc.
Brooklyn, NY

Hypotheses relating residential and individual/household contributions to mental disability are formulated and tested utilizing Mental Health Demographic Profile System data and other information. The hypotheses are concerned with the relative contributions of factors such as social class/rank of residential environment and individual social rank to psychological health. Variables such as ethnicity and mobility, homogeneity, and overcrowding in the area are considered.

Strategy Development Project for a Statewide Community Support System
278-77-0109; $162,480

Arizona, State of
Phoenix, AR

A 3-year strategy for developing statewide community-based care for mentally and emotionally disabled adults in Arizona is developed. An organizational unit responsible for facilitating the development is established, and a participatory process to provide a complete assessment of relevant needs and resources is organized. An analysis is made of the implications of community support goals for future manpower development, technical assistance, and training efforts.

In 1979, a Community Support System (CSS) Action Plan is completed. Other tasks include: the refinement and implementation of Year 1 of the Plan; documentation and evaluation of the implementation activities, development of a management system which integrates both programmatic and administrative elements into a process for monitoring; and development of implementation and evaluation strategies, models, methods, and materials which will be useful to other States attempting to develop and improve their CSSs.

Rehabilitation of Psychotic Mothers and Their Children
MH 28143; $122,944

Dincin, Jerry
Thresholds
Chicago, IL

An innovative intervention program for schizophrenic and depressed (psychotic) mothers and their children below age 5 aims at returning the mother to the community. Aftercare services include provision of vocational training, social rehabilitation, and a specific program designed to prevent rehospitalization; individual, group and family therapy; and continuing education. This is combined with a therapeutic nursery school, in which specially trained teacher therapists foster the child's working through of his mother's disturbance while providing remedial training in such areas as reality testing. Additional work is carried out with mother and child together. Mothers and children in this intensive, time-limited—12 to 15 months—program are compared with mothers and children in a minimally treated home-visit group and with a control group in the community. This is done at the beginning and conclusion of the intervention and at the 1-year followup. Assessment is made of changes in maternal personality and reduction of psychopathology and success in adapting to major adult social roles, as well as in cognitive and socioemotional functioning among the children and changes in the quality of the mother-child interaction.

Planning and Implementing a Community Support System (CSS)
MH 35646; $342,470

Director
Department of Human Services
Washington, DC

A community-based support system is further developed and implemented for the chronically mentally disabled in one catchment area of the city. A strategy is designed for the development of a similar system on a citywide basis. The components of the program are: identification of the target population; 24-hour crisis service assistance in securing benefits and entitlements; psychosocial rehabilitation services; supportive services; medical and mental health care; support and assistance to families and community; involvement of concerned citizens; protection of clients' rights; and case management. The program is designed to provide residential housing opportunities for clients as an alternative to institutionalization. Planning encompasses interagency cooperation, peer review, effective training of case managers, and an employment program for clients which includes vocational rehabilitation. Attention is focused on minority participation in the demonstration program, with emphasis on recruiting a Spanish-speaking staff to insure that the special mental health needs of the Hispanic community are met.

Service Needs of Children at Risk for Schizophrenia
MH 30921; $30,307

Erlenmeyer-Kimling, L.
New York State Psychiatric Institute
New York, NY

Services in the form of advisory screening, referral, and followup are provided to families who are participating in longitudinal research on children at risk for schizophrenia. Systematic assessments are made of: the needs of such children and their families during the children's latency and adolescence years, the availability of resources to meet these needs, the effectiveness of contact with these resources, and the value of a service function in the framework of high-risk research. Assessment of the effectiveness of the program for each family takes place at the end of 3 years, together with a determination of the relationship, if any, between life stress events and problems requiring consultation. Most of the children in this study are offspring of one or two schizophrenic parents.

Strategy Development Project, Statewide Community Support System (CSS)
278-77-0108; $306,932

Georgia, State of
Atlanta, GA

This contract with the State of Georgia Department of Human Resources is part of a National Institute of Mental Health initiative, the Community Support Program (CSP), designed to stimulate States in developing community-based care for mentally and emotionally disabled adults. State level objectives are to: establish, under the State mental health system, a unit responsible for facilitating the development of community support systems; identify and promote concerted action toward community support goals on the part of a broad-based constituency of key groups and decisionmakers within the State; organize a participatory process that provides an assessment of community support systems within the State; analyze the implications of community support goals for future manpower development efforts; and prepare a 3-year interagency State/community support strategy delineating specific objectives, responsibilities, resource requirements, incentives, and sanctions. National level objectives are to: demonstrate methods by which a State mental health agency can provide leadership in planning and mobilizing community support systems; collect and disseminate data on quality, availability, utilization, and funding sources; document specific achievements and problems encountered in the strategy development process, and analyze the implications for other States and for national policy; and identify obstacles within existing Federal, State, and local legislation and policies, and develop methods to overcome such obstacles.

Beginning in 1979, a State CSS Action Plan was prepared, completed, initiated, and evaluated. Also, a management system which integrates both programmatic and administrative elements into the process monitoring is developed.

Teaching Home for Developmentally Disabled Children
MH 32803; $195,714

Lovaas, O. Ivar
University of California
Los Angeles, CA

A series of treatment facilities called Teaching Homes are developed as alternatives to State hospital care for developmentally disabled (autistic and schizophrenic) children between the ages of 2 and 18 years. A short-term training program is also developed for training couples to be professional teaching parents for these homes, which are in residential communities. The program includes a home correspondence course for training the children's natural parents to assume the role of trainer for their own child to make it possible for the child to eventually be returned to living at home. The course covers the application of operant conditioning principles to a home with children, measurement and graphing, and devising and applying token economies. Home visits by the trainer and frequent communication by telephone between parents and trainer are a part of the program.

Community Support System Program for Chronically Mentally Disabled
MH 34874; $249,764

Maine, State of
Augusta, ME

Maine is continuing to provide a statewide community support program for the chronically mentally disabled. Project efforts continue in resource development, regional planning, consumer and citizen participation, systems advocacy, interagency collaboration, community support program concept dissemination, and skill development. Technical assistance relevant to transitional employment, vocational rehabilitation, alternative housing, transportation, and crisis intervention is furnished.

Community Support System (CSS) Strategy Development and Implementation Project
MH 35812; $414,665

Massachusetts, State of
Boston, MA

Massachusetts is continuing to develop a statewide community support system (CSS) for the chronically mentally disabled. All aspects of the Brockton CSS demonstration project—including housing, employment, interagency collaboration, and patient participation—are refined and expanded. Technical assistance is provided to three development sites: Cape Ann, Metropolitan Beaverbrook, and Coastal Communities Counseling Center. Federal, State, and local obstacles, opportunities, and funding sources for CSSs are identified; and State level policy modifications are developed. A broad base of CSS constituency groups receive education and technical assistance. Formalized training programs in CSS services are established.

Soteria II: An Alternative to Hospitalization
MH 25570; $77,089

Menn, Alma Z.
Mental Research Institute
Palo Alto, CA

Soteria II, an extension of an earlier program, Soteria I, which provided developmental-crisis treatment for schizophrenics, is under evaluation. The present study compares Soteria II subjects with control subjects. The experimental subjects are approximately 60 young—15 to 30 years old—unmarried, first-break schizophrenics selected to participate in the developmental-crisis orientation community residence. The control subjects are schizophrenics treated in the usual community mental health center programs. In the Soteria program, the crisis is taken seriously yet not stopped or repressed with phenothiazines. It is integrated into the continuity of the person's life; and the individual is allowed to experience the crisis in the context of a warm, empathetic, supportive, human relationship. Specially trained nonprofessionals using this method are studied and compared with other mental health personnel. Their relationships and interactions with patients are correlated with outcome. The progress of the two groups is evaluated from data obtained at admission, discharge, and 6, 12, and 24 months after admission.

Community Support Systems (CSS) Strategy Development and Implementation Project
MH 35823; $240,693

Michigan, State of
Lansing, MI

The State mental health staff, working with community mental health personnel, facilitates the development and expansion of a comprehensive system of community support services for the chronic mentally ill in Michigan. A series of workshops are planned to meet program development needs as identified by the line worker and consultant staff. Plans also include the active involvement of consumers and advocates in the planning process and special research projects on the mental health needs of minorities and women. Alternative treatment programs are proposed along with independent living proposals, community residential services, and mental health models for jail populations. Mainstream public and private funding resources for the community support systems are identified and secured.

Strategy Development Project, Statewide Community Support System (CSS)
278-77-0080; $308,334

New Jersey, State of
Trenton, NJ

This project develops a strategy for a statewide Community Support System (CSS). On the State level, this involves establishment of an organizational unit responsible for facilitating development and improvement of a CSS; promotion of a broad-based constituency within the State; completion of an assessment of CSS needs and resources within the State; an analysis of future manpower development, technical assistance, and training needs; and preparation of an interagency State CSS strategy. On the national level this involves: demonstration of methods by which a State mental health agency can provide leadership in mobilizing efforts toward CSSs; development of methods and materials for dissemination to other States attempting to improve CSSs; collection of baseline data on quality, availability, coordination, costs, and funding sources for CSS components at the beginning of the planning process; documentation of specific achievements, spinoffs, and problems encountered in the strategy development process; and clarification of resource requirements for CSSs, identification of obstacles within existing Federal, State, and local legislation and policies, and development of methods to overcome such obstacles.

Beginning in 1979, a State CSS Action Plan is prepared, completed, initiated, and evaluated. Also, a management system which integrates both programmatic and administrative elements into the process of monitoring is developed.

Objective Assessment in Mental Institutions
MH 25464; $64,120

Paul, Gordon L.
Illinois Department of Mental Health
Decatur, IL

An effort is made to extend programmatic developments from a previous long-term comparative study of institutional treatment by extending the evaluation of reliability, utility, validity, and training procedures relating to two observational assessment instruments—the Time Sample Behavior Checklist (TSBC) and the Staff-Resident Interaction Chronograph (SRIC). Test subjects include the full range of institutionalized adult functional psychotics in samples of State hospital wards, mental health center units, and sheltered-care homes. An effort is made to determine the limits of generalizability and parametric characteristics of observers. Self-contained manuals, videotapes, and observer training procedures are developed and evaluated in preparation for dissemination of TSCB and SRIC to other clinical and research workers. A further study is made to determine the process and social environment of chronically institutionalized patients placed in sheltered-care facilities. These patients are from three treatment groups of the previous comparative study. They are studied during the second year in the community after direct contact by clinical research staff has terminated. Data are collected on a minimum of 440 patients and a minimum of 330 staff by trained observers. Subjects are adults between the ages of 18 years and 64 years. Performance sites are the Adolph Meyer Center in Decatur, Illinois and other mental health facilities in Illinois.

Deinstitutionalization and the Sheltering Capacity
MH 30305; $179,260

Scheff, Janet
Columbia University
New York, NY

Activities in a community that promote the mental health of deinstitutionalized mental patients are studied. Both formal service activities and informal social interaction activities are described in terms of their sheltering/supporting or rejecting/nonsupporting characteristics. Indicators of the degree of community support which any given neighborhood will provide to former residents of State hospitals are proposed and examined, and strategies for increasing a neighborhood's sheltering capacity are considered. The research involves participant observation of everyday behavior in four neighborhoods, and an examination of agency records.

Patient Versus Staff Day Treatment Programming
MH 33116; $108,750

Sigman, Eric
Postgraduate Center for Mental Health
New York, NY

The relative efficacy of alternative treatment programs for psychiatric patients within a psychiatric day center is examined. The study compares a program in which goal setting and daily activity scheduling in the day clinic are primarily generated by the patient with an alternative program in which these tasks are performed by counselors. The effects of the two programs are assessed through psychiatric rating scales and by comparing the number of patients terminating treatment for positive reasons (for example, employment) and for negative reasons (for example, relapse or rehospitalization). The relationship of patient characteristics obtained from psychiatric rating scales and biographic/demographic data to treatment effectiveness is also analyzed. Of the approximately 200 previously hospitalized clients participating in the study, 70 percent have a diagnosis of schizophrenia.

State/Local Community Support Systems (CSS)
MH 35647; $350,000

South Dakota, State of
Pierre, SD

The State of South Dakota is continuing to develop a statewide community support system for the chronically mentally disabled. The demonstration sites are located at Huron and Mitchell.

Mathematical Models for Psychiatric Care Delivery
MH 32723; $62,280

Stout, Robert L.
Butler Hospital
Providence, RI

An operations research approach is utilized for developing and testing mathematical models for predicting length of stay in psychiatric hospitals. The research data used are patient-problem oriented, although diagnostic data are used if they are found to be predictive. The statistical analysis includes not only advanced linear models, but also nonmetric approaches, life table methods, and nonlinear models.

Community Support System (CSS) Strategy and Implementation
MH 35825; $500,000

Texas, State of
Austin, TX

Texas is continuing to provide a statewide community support system for the chronically mentally disabled. The system is planned and implemented around collaboration among the State hospitals, community mental health centers, and Fairweather Lodges. All aspects of the Wichita Falls demonstration project and the Fort Worth and Dallas program development sites—including housing alternatives, transitional employment opportunities, interagency collaboration, and consumer participation—are refined and expanded. Opportunities and funding sources for community support systems are identified, as well as obstacles to system development. Education and technical assistance are provided to a broad base of community support program constituency groups, and formalized training programs are established. Consultation and assistance are provided to the Texas Research Institute on Mental Sciences in the development of a manpower planning and development program.

Division of Special Mental Health Programs

Fanon Mental Health Research and Development Center (FRDC)
MH 25580; $285,419

King, Lewis M.
Charles R. Drew Postgraduate Medical School
Los Angeles, CA

A multidisciplinary, black research and development center focusing on mental health is established. Research concentrates on the black family. Family growth and development are studied, including the patterns of child rearing, family organization, survival styles, and political and social evolution. The various influences on family and individual behavior are observed, as well as the physiological bases of behavior. In social planning and organization regarding the growth and development of black organizations, methods of community development such as urban planning and law enforcement, and the impact of social and political change are considered.

In 1979, the major study is focused on stress, hypertension, and depression in black families. A sample of 400 volunteers, 25 to 55 years of age, and their families living in Los Angeles County are subjects of the 5-year, longitudinal survey. Biochemical and psychological relationships between psychotropic medication and stress in the treatment of schizophrenic blacks are explored in a pilot study. A second pilot study is concerned with developing a taxonomy of black family environments. The process of social change in an urban poverty community and the implications of these changes on marital adjustment are examined. A third pilot study is conducted on mental health service delivery to black communities and involves five community mental health centers, located in Boston, Kansas City, Atlanta, Los Angeles, and San Francisco. A consortium convenes to explore the mutual research and evaluation needs of these urban areas in relation to the black populations.

Interactional Factors in Antisocial Behavior
MH 31353; $101,917

Mednick, Sarnoff A.
University of Southern California
Los Angeles, CA

The researcher is synthesizing and expanding ongoing studies now in progress concerning the role of genetic and environmental factors in the etiology of antisocial behavior. Adopted children in Denmark are studied and comparisons made of their backgrounds as related to criminal behavior, including the influence of biological and adopted fathers. Information is collected from the National Police Register; and concordance studies are completed with regard to factors such as socioeconomic status, place of birth, and type of crime. Additional studies of sets of twins investigate psychophysiological implications and correlate cognitive tests, interviews, and an avoidance learning experiment. A large number of youth with well-documented life histories are examined, and the delinquents are compared with the nondelinquents. An analysis of high-risk children who are born of schizophrenic mothers is extended. A study of the incidence of criminality in Copenhagen is made based on data previously collected on individuals sentenced in that city during a 2-year period. The longitudinal data and analyses cover individuals from birth to mature adulthood and include 14,000 adoptees, 13,000 twin pairs, 9,000 delinquents, 200 high-risk children, and 58,000 biological and adoptive parents.

Neuropsychiatric Diseases: Transmitters and Receptors
MH 30626; $82,725

Yamamura, Henry I.
University of Arizona
Tucson, AZ

Changes in neurotransmitter receptors and metabolic enzymes are investigated in certain neurological diseases found in elderly and middle-aged people (Huntington's chorea; Parkinson's disease, and Alzheimer's disease) and in schizophrenia. Initial studies of acetylcholine, γ-aminobutyric acid, or dopamine binding are perfomed utilizing rat brain tissue. Cerebral spinal fluid of patients with neurological disease is analyzed, and postmortem brain tissue is examined.

Office of Program Development and Analysis

Evaluation of the Community Support Program (CSP): Analysis of Needs Assessment Methodology

278-79-0036; $39,175

Human Services Research Institute
Washington, DC

The needs of the chronic, severely mentally disabled adults residing outside of institutions are reviewed and summarized for the 20 federally funded State Community Support Programs. Needs assessment methodologies utilized by each of the States are reviewed. New methodologies suitable for use at the State and national levels are developed.

Collaborative Data Collection and Analysis for Community Support Program Demonstration Projects

278-79-0031; $18,533

Market Facts, Inc.
Washington, DC

A recently developed client service utilization data instrument for the use of local Community Support Program demonstration projects is pilot tested. The Community Support Program demonstration projects are intended to stimulate the development of integrated systems of community-based care and services to meet the needs of chronic, severely disabled adults residing outside of institutions. The feasibility of obtaining reliable and valid data for use in future large-scale, multisite surveys is determined. A final data collection package is prepared.

Back Issues Available

Two back issues of the *Schizophrenia Bulletin* are still available to requesters:

Schizophrenia Bulletin, No. 5, Spring 1972.
(Issue theme: Childhood Psychoses)

Schizophrenia Bulletin, Vol. 4, No. 2, 1978.
(Assorted topics)

If either or both of these issues are missing from your collection, let us know, and we will send you a copy free of charge. Requests for back issues should be sent to the following address: Center for Studies of Schizophrenia, National Institute of Mental Health, Alcohol, Drug Abuse, and Mental Health Administration, 5600 Fishers Lane, Room 10-95, Rockville, MD 20857.

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In December 1969, the first issue of the *Schizophrenia Bulletin* was issued on an experimental basis. Its appearance was followed over the next 4 years by 10 additional experimental issues. On September 25, 1974, permission was granted by the Office of Management and Budget for the *Bulletin* to be established as a regular quarterly publication. The Secretary of Health and Human Services has determined that the publication of this periodical is necessary in the transaction of the public business required by law of this Department. Use of funds for printing this periodical has been approved by the Director of the Office of Management and Budget through May 15, 1983.

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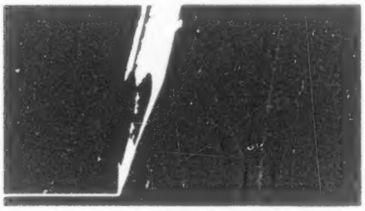

Individuals interested in submitting materials to the *Bulletin* should correspond with:

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Rockville, MD 20857

The editors will consider critical reviews of the literature, articles reporting original observations in laboratory or clinical research, short reports of preliminary or negative research results, and theoretical dissertations and other essays. News items describing research and training programs or reporting professional activities in schizophrenia are also welcome. Photographs of art done by current or former mental hospital patients may be submitted for possible reproduction on the cover of the *Bulletin;* the artist must be willing to grant permission for publication of his work, but his anonymity will be preserved if he so wishes.

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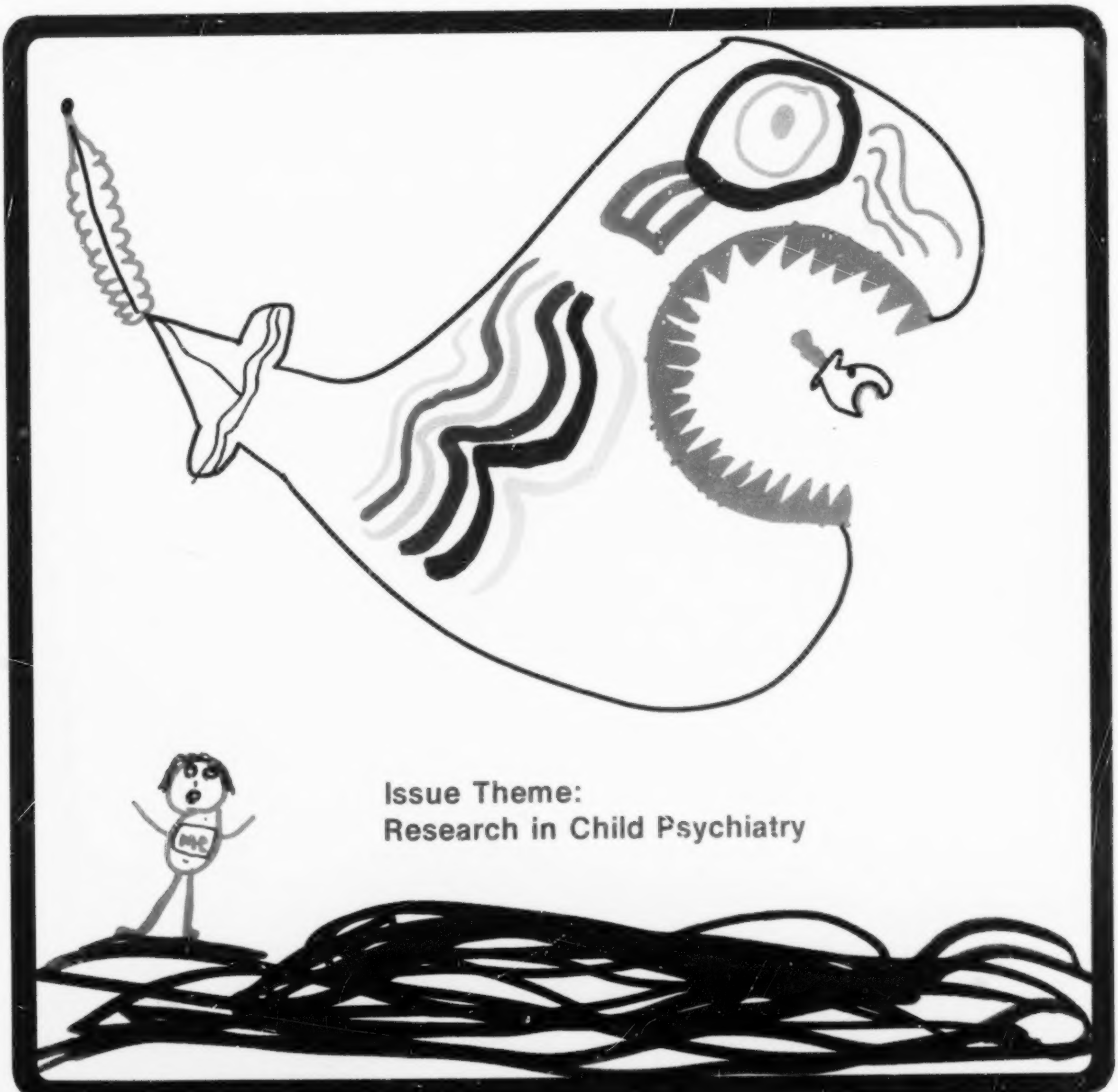

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Research in Child Psychiatry

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Schizophrenia Bulletin National Institute of Mental Health

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This is Volume 8, No. 2, of the *Schizophrenia Bulletin,* a quarterly periodical prepared by the Center for Studies of Schizophrenia, National Institute of Mental Health, Alcohol, Drug Abuse, and Mental Health Administration. The *Bulletin*'s purpose is to facilitate the dissemination and exchange of information about schizophrenia and to provide abstracts of the recent literature on the subject. Material contained in the *Bulletin,* including viewpoints expressed by NIMH staff members, does not necessarily reflect the opinions, official policy, or position of the National Institute of Mental Health. All articles appearing in the *Bulletin,* except where otherwise noted, are in the public domain and may be reproduced or copied without requesting authors' permission.

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About the Cover

The painting that appears on the cover of this issue, "Whale Swallowing a Little Fish," was done by an 8-year-old boy with a tic syndrome, who was experiencing the acute stress of parental divorce. He felt small, passive, and helpless.

The art work was provided to us by Dr. Donald J. Cohen, Guest Editor of this issue of the *Bulletin,* of the Child Study Center, Yale University School of Medicine, New Haven, CT.

Preface

The appearance of this issue of the *Schizophrenia Bulletin* marks an important phase in the development of the field of research in child and adolescent psychopathology. In its preparation, the Center for Studies of Schizophrenia has been joined by the Center for Studies of Child and Adolescent Psychopathology, which has recently been established in the Clinical Research Branch of the Division of Extramural Research Programs at the National Institute of Mental Health. Furthermore, this is the first time that an entire issue has been devoted to children and adolescents. From time to time over the years, important articles in this area—for instance DeMyer, Hingtgen, and Jackson's review article on infantile autism (Vol. 7, No. 3, 1981)—have appeared, but never before has the sense of growth in the field been such that it seemed warranted to devote a complete issue to what was happening in it.

The Center for Studies of Child and Adolescent Psychopathology may need some introduction to regular readers of the *Bulletin*. The Center came into being in October 1980 as a part of an overall effort to provide the extramural research activities of the Institute with a focal emphasis that was consistent with the most recent developments in the mental health sciences. The Center was designed to stimulate the development of rigorous investigative approaches to the major psychopathological disorders of the first two decades of life. It has both grants management and coordinating functions in NIMH. It acts as a focal point for the broad range of child-related research activities that occur within the Institute. It carries out a continuing review of developments in the field and seeks to identify gaps in knowledge and obstacles to investigative progress. Through a variety of workshops, conferences, and other mechanisms, the Center seeks to stimulate the development of important aspects of its assigned area of interest. In its grant activity, the Center is currently supporting 34 projects at a level of approximately 4.5 million dollars. Applications for grant support compete along with other grants submitted to the Institute, and funds are awarded in accordance with the action of appropriate peer review committees and the final decisions of the National Mental Health Advisory Council. Among the 34 projects now supported by the Center, 11 are High Risk Schizophrenia and Depression projects, 7 deal with Attention Deficit Disorder/Hyperactivity, 7 with Childhood Depression, and 5 with Infantile Autism. The scope of the Center's programs includes etiology, phenomenology, diagnosis, course, outcome, and prevention. Treatment research is funded through other branches in the Division of Extramural Research Programs.

The Yale articles contained in this special issue exemplify the best of what is taking place in child psychiatry today. In the depth and richness of their investigative interests, they are typical of the upsurge in research enterprise that has been increasingly evident over the past 5 years in the *Journal of the American Academy of Child Psychiatry* and at every national meeting where children's disorders are of concern. The papers by Cohen, Young, Shaywitz and their associates are alive with a renewed curiosity about old puzzles. They are rooted in clinical tradition, but the methods that they make use of include the most sophisticated biochemical, neurodevelopmental, epidemiological, and statistical approaches now available. The work that they represent derives from productive new linkages with adult researchers and draws on the efforts of an interdisciplinary team which is deeper and more varied, especially in the neurosciences and pediatrics, than the old professional triumvirate that contributed so much to child psychiatry's development. From the efforts at Yale and similar academic centers around the country, new facts about the serious mental conditions of childhood and adolescence are emerging at an increasing rate, and there are new ideas being formulated to explain those facts that suggest even more exciting lines of investigation. The reader of these articles will find much of the excitement of the future contained within the pages that follow.

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Upcoming Autism Meeting

The National Society for Children and Adults With Autism (NSAC) will hold its 14th Annual Meeting and Conference in Omaha, Nebraska July 6 through July 10. The theme of the 1982 conference is "Autism: A Family Affair." Specialists in special education, research and medicine will be featured.

Topics will include presentation of new research and concepts in autism and roundtable discussions by parents and professionals. There will be special emphasis on adolescents and young adults with autism and the problems that face them in the community. Also highlighted will be teacher training and organized advocacy sessions.

Continuing education units will be offered at Creighton University in Omaha.

For more information, contact NSAC, Suite 1017, 1234 Massachusetts Ave., N.W., Washington, DC 20005. Or call (202) 783-0125.

Clinical Research in Child Psychiatry—Methods and Strategies

by Donald J. Cohen

Abstract

Research methods in child psychiatry are derived from many disciplines—epidemiology, genetics, neurochemistry, pharmacology, electrophysiology, psychology, linguistics, and analytical chemistry—as well as several branches of medicine, particularly pediatrics, neurology, and psychiatry. The application of methods must be informed by the knowledge and concerns which emerge from the clinician's authentic clinical engagement with children and families. Research strategies require the definition of specific questions which can be addressed by discrete studies as well as the progressive integration of findings and perspectives. Systematic clinical investigations require institutional supports—opportunities and enticements for young investigators, long-term stability of research groups, and ease of collaboration among specialists.

Clinical research in child psychiatry has entered a new and industrious phase of development. It is characterized by emerging orderliness and rule-governed activity, by the desire to categorize and organize data, and by an effort to see phenomena from varying perspectives. The flair of the child psychiatric pioneers of previous decades for sweeping clinical generalization and dynamic acuity is now being complemented by the slow, cautious marshaling of evidence and the use of psychobiological and other scientific methods. Advances in biology, biomedical research, and various disciplines of behavioral and cognitive sciences have provided clinical researchers with sensitive approaches and broadening theoretical scope.

This issue of *Schizophrenia Bulletin* aims to exemplify the spirit of clinical research in child psychiatry by focusing on methods and strategies. Multiple approaches may be used to explore central nervous system function and behavior, and the integration of diverse viewpoints is required to achieve an increasingly comprehensive picture of disorders and of individual children, as described in the overview chapter by Young et al. The study of one class of disorders—attention deficit disorders—highlights the relations between basic behavioral and neurobehavioral research, on the one hand, and clinical dysfunction, on the other (Hunt et al.). The methods of epidemiology (Jagger et al.) and behavior and population genetics (Pauls and Kidd) can define syndromes and provide suggestions about cause and natural history. For neurochemical research with children, sensitive analytical methods using small samples are required; new analytical chemical methods are ideally suited for such studies (Anderson and Young). The response of groups of children to medications may suggest aspects of underlying disturbance. Increasingly rigorous clinical pharmacology can guide clinicians in the use of medications with the most seriously disturbed children (Mikkelsen). Disturbances in bodily functioning have a major impact on development, and studies of pediatric illness and psychosomatic correlations can have broad in-

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terest in illuminating the relations between bodily integrity, self-esteem, motivation, and cognitive performance. Children with endocrine disorders may be a particularly good group for dissecting these relations (Abbott et al.).

No area of development is more intrinsically human, or more commonly affected in early-onset disorders than linguistic functioning. Recent developments in psycholinguistics provide clinicians with a framework for understanding the emergence of communicative competence and ways in which language development may be altered in different clinical syndromes (Paul and Cohen).

Clinical research of all types—neurochemical, genetic, pharmacological, descriptive—requires careful measurement of behavioral and clinical phenomena. During the past years, rating instruments and structured interviewing procedures have become parts of the clinical researcher's repertoire in all branches of psychiatry. Clinical data systems concerning development and parental and school histories are essential for clinical research in child psychiatry, and are particularly well developed for children with learning and attentional difficulties (Shaywitz). These disorders also raise important conceptual questions about the relation between physical signs and behavior (Shaywitz). Numerous laboratory tests of behavioral performance and clinical neuromaturational examinations have been used with children for assessment of aspects of motor functioning. The relations between measures and their clinical validity and usefulness remain, however, open questions (Harcherik et al.).

The series of articles in this issue is generated by a collaborative group of investigators who have shared methods, concepts, patient populations, and questions over the course of a decade. What can be learned from the history of this and similar research efforts?

Contemporary research in child psychiatry is marked by the need for collaboration between basic and clinical investigators and among investigators with different clinical research competencies. The problems being studied and the questions being asked are too complex for the solo investigator using only one or a few methods. There is a necessary interaction between levels of organization—from genetics through molecular and pharmacological levels of analysis to studies of children in the context of family and school—in which questions and concepts move from the basic laboratory to clinical testing and from clinical observation back to the laboratory. In the place of ideological debates, clinical investigators today are essentially eclectic and empirical—they are interested in well-framed hypotheses, methods for producing information, and the challenging, as well as the support, of ideas. In place of the old schools—e.g., nature vs. nurture, biology vs. environment, description vs. dynamics, pharmacotherapy vs. psychotherapy—clinical investigators are more likely to give each domain its own place in an interactive model and to recognize the mutuality and complementarity of approaches.

Institutionally, clinical research in child psychiatry only recently has emerged as a powerful force. During its first decades, child psychiatry as a profession was characterized by its essential clinical thrust and had its roots in dynamic principles, a social service orientation, and good, pediatric, child-oriented common sense. In most academic centers, child psychiatry was represented by one or two "full-time" academicians and very part-time consultants whose major responsibilities were training and clinical supervision. Laboratories, research wards, full-time investigators, research cohorts, basic scientists—the resources and personnel of clinical investigation—were essentially foreign to most child psychiatric programs long after they had become embedded in pediatrics and general psychiatry, the neighboring disciplines. Today, there is growing recognition within child psychiatry and increasing, if still at times ambivalent, support from outside for the tenet that child psychiatry must be based on empirical clinical research and must find its own foundations as an academic discipline. To a considerable extent, child psychiatric research has advanced by the adaptation of methods and concepts from general psychiatry, where a relative abundance of clinical investigators has been at work for several decades. The essential questions of child psychiatry, however, concern development and dysfunctions which impede its progress, and the close connections between biological and psychological development within the individual and individual development in the context of the intimate family. For an approach to these basic questions, child psychiatry needs to shape its own strategies and methods, borrowing from basic science disciplines (such as developmental psychobiology, psychology, and psycholinguistics) that are more peripheral to the interests of general psychiatrists. Also, the disorders unique to infancy and childhood remain the special province of child psychiatric investigation and call for approaches sensitive to the changes and tasks of development.

Formal child psychiatric research has tended to emphasize only a narrow segment of clinical disorders, and autism and attention deficit disorders probably have received the most attention from clinical investigators. Questions can, and should be raised about the choice of disorders that have been studied and whether other important areas of dysfunction have received relatively too little clinical research commitment. More important, however, is the fact that clinical research in autism and attention deficit disorder has provided models of investigation which can be generalized. It has been shown that clinical research is possible with children, even very disturbed children, and that such investigation is not only compatible with empathic, genuine clinical care, but may improve the quality of care. Not more than a decade ago, questions were still being raised about the feasibility and ethics of neurochemical and other biological studies with young children. Not only have multiple studies been done, they have been performed with rigor equal to that in general psychiatry. If not in quantity, then in the use of state-of-the-art methods and in overall quality, child psychiatric clinical research has kept pace with clinical research in other areas of psychiatry during the last several years.

The collaborative research group represented in this issue has used various methods: neurochemical, clinical-descriptive, psychological, linguistic, genetic, epidemiological, pharmacological, radiological, and neurophysiological. Through the use of these methods, clinical and basic researchers in other disciplines have been brought into clinical research with children. Investigators who otherwise would not have thought about childhood disorders, much less have sat in a playroom and heard a child describe in words and action the story of his life, have become fully immersed in studies of autism, Tourette's syndrome, attention deficit disorders, and other childhood difficulties. In the future, progress of clinical research in child psychiatry will depend not only on the creation of a cadre of child psychiatric researchers, but, equally, on the building of bridges which will allow investigators with other important competencies to study and learn to care about the afflictions of childhood.

Clinical research requires a network of supports. At Yale, this network has included two major institutions, in addition to the Child Study Center, itself. The National Institutes of Health (NIH) Children's Clinical Research Center (CCRC), which recently celebrated its 20th anniversary, has been the site of inpatient biological and behavioral studies; unique among the CCRCs in the United States, the Yale CCRC has always had a child psychiatric codirector and an openness to clinical research in child psychiatry. Specially trained nurses have made possible research hospitalizations of severely disturbed children. The second, more recently founded institution is the National Institute of Mental Health (NIMH) Clinical Research Center, also unique in being codirected by an equal partnership between general and child psychiatry. The Mental Health Clinical Research Center (MHCRC) has provided the conceptual and empirical links between clinical research with adults and children, the developmental perspective on all disorders, and the laboratory and methodological resources that are essential to contemporary investigation.

In contrast with studies in the basic science laboratory, clinical research is dreadfully expensive. A single data point on a curve may represent literally dozens of hours of clinical evaluation, preparation of a child and family for participation, and patient care. Studies in the basic animal laboratory may be completed in weeks; clinical projects may require years. The collaborative studies described in this issue have been funded by the NIMH and the NIH (primarily the National Institute of Child Health and Human Development; NICHD). The "glue" to hold projects together and the flexible support that makes it possible for clinical investigators to pursue exciting new leads quickly have come from several generous private foundations: The Solomon R. & Rebecca D. Baker Foundation, Inc., and the Berger Foundation, devoted to childhood autism and similar disorders, The Gateposts Foundation, which has emphasized Tourette's syndrome, and other private family foundations. Major foundations which have had inestimable impact in shaping clinical research in the United States, the W. T. Grant Foundation, the Ford Foundation, and the

MacArthur Foundation, have been generously supportive.

The studies presented in this issue represent a discourse on methods and a sampler of findings. They are presented as illustrative of an emerging orientation and an enthusiasm that are now readily apparent in child psychiatry. They also mark the first decade of a collaborative research group whose core members—Bennett Shaywitz, J. Gerald Young, Barbara Caparulo, Sally Shaywitz, myself, and collaborators—have participated in the experience of learning about the clinical phenomena, unanswered problems, and suffering of children burdened with disorders which cry out for better understanding and more clinical investigation.

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Two back issues of the *Schizophrenia Bulletin* are available to requesters:

Schizophrenia Bulletin, No. 5, Spring 1972.
(Issue theme: Childhood Psychoses)

Schizophrenia Bulletin, Vol. 6, No. 2, 1980.
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Assessment of Brain Function in Clinical Pediatric Research: Behavioral and Biological Strategies

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by J. Gerald Young, Donald J. Cohen, Sally E. Shaywitz, Barbara K. Caparulo, Mary Ellen Kavanagh, Robert D. Hunt, James F. Leckman, George M. Anderson, Jill Detlor, Diane Harcherik, and Bennett A. Shaywitz

Abstract

Psychobiological research in child psychiatry requires rigorous assessment of behavior and multiple perspectives on brain function through neurochemical, neuroendocrine, psychophysiological, and other advanced methods. The serious neuropsychiatric disorders of childhood, such as autism, attention deficit disorder, and language disorders, can be studied in complementary clinical protocols aimed at explicating patterns of behavioral and metabolic dysfunction which characterize various clinical syndromes. Clinical research with children raises sensitive ethical issues; the ethical problems can be addressed when children and families are active collaborators with the investigators and a long-term relationship is established. In this setting, participation in research can facilitate better treatment for a child. The use of novel biological strategies, such as pharmacological challenge tests, permits evaluation of the relation of specific neuronal systems to behavioral dimensions in clinical disorders. The development of a new treatment for Tourette's syndrome illustrates the integration of basic and clinical research methods.

The goals of psychiatric research in childhood are the determination of etiologies and treatment methods for specific disorders; specification of brain-behavior relationships; delineation of neuropsychiatric developmental sequences; clarification of the contributions of endowment and experience; determination of biological components of emotional states such as anxiety, arousal, attention, fear, and depression; neurobiological description of the phenomena of brain plasticity and learning; and integration of data from these different domains. Our investigative program moves toward these goals in the context of the pressing needs of the children and families carrying the burden of the most severe neuropsychiatric disorders of childhood. Research approaches, conceived in terms of fundamental theoretical goals, are framed in response to the realistic requirements of families asking for counsel and active support in determining the best care for their children. Clinical research that retains a fidelity to the child and his family is rooted in a knowledge of the family unit which is active and continuous. Our research reflects this integration of clinical and metabolic viewpoints, with the invigoration of one by the other (Cohen 1974; Young and Cohen 1979).

Severe Neuropsychiatric Disorders of Childhood

The severe neuropsychiatric disorders of childhood, phenotypically and genotypically diverse behavioral syndromes apparent during the first years of life, affect up to 3 percent of all children. Organically definable causes include structural malformations of the brain, chromosomal abnormalities, inborn errors of metabolism, anoxia, infection, head trauma, and numerous other types of inborn and acquired pathological influences on central nervous system (CNS)

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maturation. When such medically explicable disorders are excluded, the neuropsychiatric disorders consist of a broad range of syndromes of unknown etiology involving the normal unfolding of linguistic, cognitive, and social competence. In their most severe forms, such as primary childhood autism, all spheres of development may be disturbed pervasively; in less severe syndromes, one or another facet of development is more prominently involved (such as expressive and receptive language in the developmental language disorders, or the regulation of attention and motor activity in attention deficit syndromes) (Cohen 1976; Cohen, Caparulo, and Shaywitz 1976; Rutter 1977; Rutter and Schopler 1978).

Various types of neurological and metabolic abnormalities have been postulated as the basis for the disorganization, desynchronization, and retardation in maturation that characterize such severe disorders as autism and schizophrenia. The viewpoint that these disorders rest upon an organic substrate is supported by a range of suggestive evidence. The disorders sometimes are manifest during the first weeks of life, as when the parents of autistic children recognize that the child is not normally attentive to their faces or responsive to their care. The syndromes occur throughout the world, with a fairly predictable incidence (e.g., 1:3,000 live births for autism) and with a characteristic clinical presentation and natural history. Children with neuropsychiatric syndromes often have minor atypicalities on neurological examination or on electroencephalography and have a high incidence of minor physical anomalies. The response of the disorders to medication may sometimes be dramatic (as when children with the attention deficit syndromes respond therapeutically to amphetamine or those with multiple tics respond to haloperidol) and pharmacologically explicable in relation to theories of neurotransmitter function (Cohen, Caparulo, and Shaywitz 1978). The families of some children with neuropsychiatric disorders may have an increased incidence of developmental or psychiatric pathology—for example, language difficulties in families of children with autism or personality disorders in families of hyperactive, attentionally disabled children. Finally, the neuropsychiatric disorders for which no organic basis is now known often bear striking similarities to disorders of known organic causation, such as lead encephalopathy, homocystinuria, and the rubella syndrome.

Although organic factors appear to play the central role in the origin of the severe neuropsychiatric disorders of childhood, experiential factors occasionally precipitate or markedly exacerbate a child's constitutional difficulties. For most children with these disorders, eventual competence represents the complementary relations between endowment and the quality of the child's care, the degree of family stress, the opportunities for adequate stimulation, and luck. Interactions between environmental influences and CNS metabolism, and their mutual impact on natural history, remain to be investigated (Cohen 1974; Young and Cohen 1979). The children afflicted with the severe neuropsychiatric disorders might be characterized as those in greatest need of new research-based knowledge to improve their care and as those in whom a metabolic contribution to their deficit might be most likely to be specified.

Human Investigation: Ethics, Procedures, and the Family

A discussion of the ethics of clinical research might be initiated with the thought that operation of a university-based assessment and treatment program without a research component should be discouraged. The potential pitfalls of neglecting research are exemplified by the questions raised by parents in relation to the widespread use of stimulant drugs for children with attention deficit disorder with hyperactivity (ADD–H). While these drugs are useful in the short term, they are most often administered without other concurrent modes of therapy because clinicians feel such therapeutic approaches to be "outmoded" or too "soft" and time-intensive. Yet, a lack of improvement in the long-term outcome of ADD–H children treated solely with stimulants led some clinicians to feel discouraged with this treatment. A 3-year followup indicates that multimodality treatment of this disorder, in which stimulant medication is combined with one or more psychosocial therapies according to individual needs, leads to less antisocial behavior, better academic performance, and improved adjustment at home and school than in a group receiving less treatment (Satterfield, Satterfield, and Cantwell 1981). In retrospect, it does not seem surprising that treatment directed toward several areas of a child's function would be more useful than drug treatment alone. Nevertheless, if this research had not been done, unnecessarily restricted treatment methods would have continued for at least an additional decade. These complex disorders of childhood, with interacting contributions from endowment and environment, will only be understood when comprehensive and continuous research is undertaken. Without this research, children and families will be vulnerable to the oscillating interests of clinicians when seeking treatment. This is most clearly the case for children with the severe neuropsychiatric disorders.

In spite of the potential for an unhappy long-term outcome for individuals with such disorders as ADD–H, autism, and pervasive developmental disabilities, there has been a tendency to regard biological methods of assessment as too intrusive when included in a research protocol. We now wonder whether it is sensible to neglect biological research when caring for these children, in view of the severity and intractability of these disorders. Should not the child's disorder and currently favored treatment methods be carefully investigated as part of a comprehensive, humane approach to the problems of the child and family? Intensive psychotherapies represent a major intrusion into the life of a family, yet there has been an unwillingness to assess the utility of these therapies because of the difficulties such research presents. The lack of evidence demonstrating etiologies and optimal treatments for childhood disorders makes it clear that all possibilities must be scrutinized if children are to have the best care available. If urine and blood sampling and other physiological assessment techniques are acceptable procedures in serious nonpsychiatric medical disorders, then the manifest suffering and impairment attributable to the childhood neuropsychiatric disorders justifies the most comprehensive biological and behavioral research.

In our studies of children with developmental disabilities, we have adopted several methods for protecting the rights of children and families, minimizing potential patient risk, and obtaining clearly understood consent. These have included careful selection of patients; preparation of children and families; close collaboration with parents, who can room-in with children who are hospitalized; the clinical presence of the research staff directly responsible for children's care and studies; and special training of nursing and other personnel involved with research patients.

Only families who are completely able to understand the nature and purposes of our research are selected for participation. Families are not invited to join in research studies when they are undergoing unusual family stress or when they are unable to form a stable research collaboration. For those families who cannot be involved in a research collaboration, appropriate medical referrals are arranged. Families involved in research are given copies of publications. The research is described in detail during several outpatient visits, usually extending over the course of months. During the course of evaluation, the researchers review the child's previous development, reports from other professionals and schools, and results of standard laboratory and clinical evaluation procedures. On the basis of these studies, an assessment is made of the child's developmental needs and developmental disturbances. Children who are at unusually sensitive points of development (for example, who seem to be going through periods of accelerated language acquisition) are studied only with the least intrusive cognitive, language, and blood assay methods.

Children who are able to understand the protocol are asked to give written assent on specially designed forms. Parents are given copies of research protocols and encouraged to study them both in the presence of the physician and at home at their leisure. Before parents give written consent, it is determined whether they fully understand the nature and purposes of the research study to which they are consenting. When children are to be hospitalized for special studies, parents and children are encouraged to visit the specially designed Children's Clinical Research Center before hospitalization. Before procedures are performed, the nurse explains each step and ensures that the child and family understand the study.

Of all research procedures, the lumbar puncture with or without probenecid loading presents the most concern to researchers and families. In our research, lumbar puncture and cerebrospinal fluid (CSF) examination are performed only with children who are suffering from severe, lifelong disorders of unknown etiology for which there is no specific, available treatment (for example, childhood autism, aphasia, and Tourette's syndrome). For these children, lumbar puncture and CSF examination are part of an intensive, clinical evaluation of the child's extremely disabling disturbance. It is explained to the families that the results of any particular child's examination are unlikely to reveal information relevant to the child's current treatment. During the past 10 years, lumbar puncture and CSF examination have been performed on over 100 children in our studies. The most common side effects have been (1) nausea from probenecid, the medication given for 12 hours before lumbar puncture for metabolic studies of catecholamine metabolism, and (2) lumbar puncture headaches. The probenecid-induced nausea typically occurs during the last part of the probenecid loading and persists for several hours following lumbar puncture.

Blood and urine studies pose no physical threat to children. To the degree possible, the procedures are carefully described to children and are performed as thoughtfully as possible. Children are especially prepared for electroencephalograms and other procedures by research staff members, nurses, and special educators at the schools that the children attend. In our experience, the most important aspect of the preparation and performance of these studies is the presence of the child's parents and other individuals with whom the child is comfortable. With careful preparation, we have generally been able to complete studies, such as electroencephalograms, for children who have never been able to have these procedures done satisfactorily before. None of the measures of attention, vigilance, or performance are intrusive, and all have been used with young children. For these behavioral studies, there are no associated risks.

Central to our philosophy of human investigation is the idea that collaboration in research studies is not episodic. Children and families who become involved in research are part of an ongoing research collaboration. They can, of course, terminate this collaboration at any time; what is essential to the relationship is the explicit knowledge that all information will be shared by the investigator and that the goal of the research is to understand the disorder experienced by the individual child. The results of all studies are made available to families through discussion and in written form. Detailed reports are prepared for professionals involved with the child and are reviewed with the parents, who are given copies. Recommendations based on findings are shared with the family and placed in the context of the child's general care. Often, the results of the evaluation are used to help the family make decisions about special education or pharmacological intervention. Children and parents are seen following their inpatient studies on an individual basis. Regular school reports are reviewed with the families. Research reports are presented to parent advocate groups and to the staffs of schools involved with children who have been studied. Published articles are circulated to parents. In addition, there is an annual meeting to which all families involved in the research, as well as interested professionals, are invited. At this annual meeting, the progress of research during the past year and plans for the future are described.

Neuropsychiatric Research in Childhood: Clinical Assessment

Diagnosis and Development. The foundation of the research program of the neuropsychiatric investigatory group at Yale has been the detailed study of specific syndromic groups, using multiple techniques and personnel with varied professional skills. In each case we have attempted to fill in a comprehensive picture of the disorder, while at the same time recognizing individual variation and using inconsistently represented traits for the formation of subgroups. The likelihood of observing a biological homogeneity underlying a specific set of symptoms should be relatively high in a group of children with similar clinical presentations, and may differentiate them from neighboring groups along the clinical spectrum. Our method has been to weave into clinical care quantifying instruments for each of the domains of data, ranging from operational criteria for inclusion or exclusion from a given category, and behavioral assessment with reliable rating scales, through the more naturally numerical physiological and biological measures. This is particularly helpful for children who have characteristics which do not clearly place them in a specific diagnostic group. Differences and similarities to other groups are highlighted, and underlying biological continuities become visible across groups, leading to the investigation of clinical and biological dimensions cutting across diagnostic boundaries.

Diagnosis has an especially dynamic side in the childhood disorders, as it occurs in a developmental perspective. This gives particular significance to a detailed knowledge of natural history in developmental disturbances, since the recognition of a possible diagnosis at age 12 years may depend on an awareness of the outcome of an early onset disorder (so that it can be considered), and a clear sense of the major clinical components of the illness during the very early years (in order to arrive at the substantiating criteria). Childhood autism, of course, is an excellent example of such a situation, and a disorder that can lead to strikingly different outcomes during adolescence and adulthood. On the other hand, diagnosis is critically important in childhood because children with early onset disorders are one of the major groups at risk for adult disturbances; often it is possible to trace the continuity between child and adult disorders. Continuity also facilitates the discrimination of treatment effects on the childhood disorders when examined over many years in the perspective of the "natural history" of other children who were not treated. Finally, respect for heterogeneity and subgrouping within discrete diagnostic groups in childhood may increase the likelihood of recognizing identifying dimensions of behavior in the early history of a patient being examined as an adult; what did not initially look like a classical childhood disorder sometimes falls within a familiar spectrum for the diagnostician who is aware of the significance of these behavioral dimensions.

Diagnostic Assessment and Instruments. All aspects of scientific investigation in pediatric neuropsychiatry depend on valid and reliable clinical assessment. A major thrust of the clinical investigation at Yale has been the refinement of the diagnostic process for children with severe neuropsychiatric disorders (Cohen 1976; Cohen, Caparulo, and Shaywitz 1976; Shaywitz, Cohen, and Shaywitz 1978; Shaywitz 1982). These activities have included the study of diagnostic reliability (Cohen et al. 1978*a*) and of the usefulness of various procedures involved in standard evaluation procedures, such as the electroencephalogram (Waldo et al. 1978), genetic screening (Lowe et al. 1980), and computerized tomography (Caparulo et al. 1981). Yale investigators have devised new instrumentation for assessment of children's personality (such as the Childhood Personality Scale) which have achieved broad use in studies of normal and developmentally disturbed children (Cohen 1974; Dibble and Cohen 1974; Cohen, Dibble, and Grawe 1977*a*, 1977*b*) and a series of rating scales which have been used for the assessment of children with developmental disorders and examination of the relation among dimensions of behavioral disturbance and biological variables. For example, in one study, children were rated on the Behavior Rating Instrument for Autistic and Atypical Children (BRIAAC), devised by B. Ruttenberg, and the Behavior Rating Scale, devised by the Yale investigators, and a high degree of intermethod agreement was found (Cohen et al. 1978*a*). These reliable behavioral measures were then related to CSF monoamine metabolite values in autistic and other neuropsychiatrically disturbed children; important patterns were elucidated, relating behavioral competence to serotonin metabolite concentration (Cohen et al. 1980*b*).

In collaboration with the Clinical Methodology and Data Processing Unit of the Yale Mental Health Clinical Research Center, we created a new instrument for clinical and epidemiological studies of Tourette's syndrome (Jagger et al. 1982). This instrument has now become a standard part of the clinical assessment of these patients, with good agreement between epidemiological and clinical data.

Sally and Bennett Shaywitz have developed a series of instruments for obtaining consistent information about children with neuropsychiatric disorders. These parent-, physician-, and school-related instruments are based on, and replace, a series of less sophisticated forms and are state-of-the-art instruments for obtaining and recording information about children's family background, development, and current status.

Each child involved in the research protocols receives a thorough neuropsychiatric assessment and a general data base is created; depending on the specific diagnosis and protocol, additional information is added to the general data base. In the practice of neuropsychiatric diagnosis, no test or procedure can replace the detailed, lengthy, and repeated interview and examination of the child and family. In our experience, the initial evaluation usually involves 3–5 hours of assessment by a pediatric clinician, at the minimum. This face-to-face discussion, observation, and interview is supplemented by a variety of other sources of information: for example, parent forms; teacher ratings; psychological tests; neuromaturational examination; attentional measures; and neurological, metabolic, or physiological studies. The following sections describe both the general data base and the additional measures obtained for children involved in research protocols. It should be noted that the diagnostic assessment must be conducted with concern for the needs and strengths of the child and family. In some situations, the process can be completed over the course of several weeks; for other families, the pace must be slower and the procedures more limited.

Clinical interviews. An experienced pediatric clinician meets with the family and child to obtain a history of their difficulties, using an open-ended format with specific probe questions. The clinician assesses the child's gestation, delivery, first months of life, and motor, social, emotional, and cognitive development; areas of symptomatology; natural history of the disorder; responses to previous intervention; current treatment program; and family history and structure. The evaluation includes observation of the child in a free play situation, engagement of the child in structured play activities, and general assessment of cognitive, social, and emotional competence. The clinical interviews (3–5 hours) provide a general portrait of the child's development in the context of genetic, experiential, familial, educational, and social factors. Data from this evaluation include a narrative statement covering the various areas noted, a diagnostic formulation, a specific *DSM–III* (American Psychiatric Association 1980) diagnosis, and rating scale information.

Clinical rating scales. Accurate and precise assessment of behavioral dimensions occurring across syndromes is the fundamental requirement for a more rational clinical understanding of childhood disorders. The use of clinical rating scales has increased the orderliness of research and the multiaxial system is essential for understanding the complex relations between symptom patterns that may appear in various combinations and with differing degrees of severity. In previous research we developed methods for parental and clinical reports on children's competence (in areas such as sociability, attention, and language), parent-child relations, and family stress (Dibble and Cohen 1974; Cohen, Dibble, and Grawe 1977*a*, 1977*b*). These measures have been used with normal and developmentally disturbed children. In clinical research studies, we have developed clinicians' rating scales for the major dimensions of disturbance in childhood psychosis (Children's Behavior Rating Scale), and have performed first-phase reliability studies (Cohen et al. 1978). In current studies, children are involved in various structured and nonstructured tasks and their behavior is assessed using newly devised rating scales (e.g., Achenbach's Child Behavior Checklist) as well as measures which have achieved broad use in child psychiatry (such as the Connors symptom checklist). In addition, the Kiddie–SADS, a structured interview particularly appropriate for higher level children with affective disorders, may become an important aspect of methodology in protocols involving children with attentional, cognitive processing, and affective disturbances.

Parent reports. During the course of the first evaluation interviews, the family is asked to complete detailed forms about the child's history and current status and his specific involvement with academic institutions. These forms include the Yale Neuropsychoeducational Assessment Scales (Shaywitz 1982) and other scales.

Physical and neurological examination. All children receive a thorough general physical evaluation. Specific neurological examination includes assessment of the general neurological status of the child, a neuromaturational examination, and examination for minor physical anomalies. This battery of instruments has been validated with a cohort of normal and developmentally disturbed children (Shaywitz 1982).

Cognitive and language evaluation. The more severely impaired children are often unable to work with clinicians in unraveling the puzzles of their disorders. This led to the development of evaluation strategies which accurately portray the patients' cognitive, linguistic, social, and emotional functioning without requiring self-reporting by the patient. The most productive method of behavioral study has coupled clinical research interviews with home and school observations and individual sessions of psychological testing. The interviews demonstrate the child's spontaneous behavior in a situation which becomes increasingly familiar to him. They are repeated on several occasions, with the child's family present in order to interpret the child's responses. After the child is maximally engaged, cognitive and language tests are selected according to the child's needs. The measures of general cognitive functioning are standardized and commonly used in clinical assessment, but the method of administration is modified in response to the child's capabilities. The assessment instruments include the Wechsler Preschool and Primary Scales of Intelligence, Wechsler Intelligence Scale for Children-Revised, and Arthur Adaptation of the Leiter International Scales of Performance (traditionally used for children with hearing impairments or severe motor impairments such as in cerebral palsy, and used by us with subjects with language disorders ages 2 years through adulthood).

It is necessary to supplement one or another of the above measures with additional psychometric assessment. The following are used to complement the basic intelligence battery or to provide a cross-validation of particular areas of functioning: McCarthy Scales of Intelligence, Yale Developmental Schedule (combines observation of object manipulation, motor skills, and object relations with testing of problem-solving abilities and language comprehension), and the Peabody Picture Vocabulary Test. Measures of language development include the Sequenced Inventory of Communicative Development, the Receptive-Expressive Emergent Language Scales developed by Bzoch-League (a detailed, 120-item inventory of chronologically sequenced questions filled out by parents for all children with language impairment), and the Illinois Test of Psycholinguistic Abilities.

The tests of cognitive, language, and perceptual-motor competence are supplemented by tests assessing academic achievement. Such tests, which are especially important in the assessment of children with attentional and cognitive processing disturbances, and in the evaluation of the impact of medication, include the Wide Range Achievement Test, Grey Oral Reading Test, and the Woodcock-Johnson Achievement Tests.

This group of cognitive, linguistic, attentional, and achievement measures yields both summative and process measures of children's underlying competence and performance. Measures are operationally defined, normalized, and quantitative. In addition, careful observation of children during the process of formal testing can reveal cognitive strategies, emotional responses, defensive operations, and overall approach to tasks and to the tester that can greatly enrich the observations of the less structured interviews.

Behavioral measures of attention, perception, and movement. The assessment of complex states such as attention is based on the characteristics of the group of children being evaluated. Pervasively disturbed children, who are often nonverbal and who have a restricted range of activities within which they can be cooperative, require discrete tasks preselected with their capabilities in mind. Other children have subtle impairments which are more readily elicited in a comprehensive, well-standardized battery of test items. Our range of behavioral assessment items is grouped into those that may be administered to all children, even the most profoundly disturbed, and a standardized test battery that can be used for normal and less severely impaired children.

1. Reaction time and continuous performance. Difficulties in focusing and maintaining attention are found in a variety of psychiatric disturbances in children and adults (Silverman 1964; Mostofsky 1970). Attention, arousal, and unusual sensitivities have been particularly prominent theoretical issues in the study of children with early onset psychoses such as childhood autism (Ornitz and Ritvo 1976). Detailed analyses of attentional processes in autistic and other severely disturbed children have been impeded by difficulties associated with the children's behavioral problems, such as hyperactivity and lack of cooperation. To assess arousal, attention, and perceptual processing, investigators have made use of a variety of nonverbal, physiological, and behavioral measures.

Two types of psychological tasks which assess processes are reaction time measures and tasks which require continuous engagement. In reaction time studies, a child is presented with a stimulus (e.g., a tone, light, or particular geometric form) on the occurrence of which he must respond (e.g., press a button) as quickly as possible. Dependent measures include: latency to respond (usually in the range of 300 msec for normal children in response to a light); errors of omission (where child did not respond); and errors of commission (responses without the presentation of the stimulus). Various factors influence reaction time performance, including initial motivation, habituation, training, presence of a warning, and nature of the stimulus. In continuous performance tasks (CPT), a child must perform an action (e.g., keep his finger on a moving knob or respond to a particular geometric shape when it is flashed on a screen) over long periods of time. Dependent measures are similar to those in reaction time which can be conceived as a type of CPT.

Care must be exercised when testing for attentional capabilities in children with severe neuropsychiatric disorders. The deficits of cognitive and social function in these children may mask the underlying attentional capabilities and deficits. In many cases it is necessary to train children on tasks used to test attentional competence. In order to make these studies possible, we have established a laboratory at Benhaven, our collaborating school for autistic and communication-impaired children, incorporating our studies into the daily curriculum of the children. In this fashion we are able to study children's reaction times to auditory, visual, and tactile stimulation repeatedly, thus obtaining data that are representative of a child's competence by taking into account day-to-day variation in performance. Also this type of training maximizes performance on the tasks during psychophysiological monitoring and enables a more refined analysis of the relationship between performance and attention.

2. General attentional, cognitive, and perceptual-motor tasks. Fine-grained, operationally defined measures of perceptual and attentional function are essential for clarifying diagnostic subgroups and the relations between domains of disturbances. As part of our multidisciplinary research activities, we develop new measures as well as use standardized tasks involving attention, perception, and motor control.

Tasks are selected to assess fine motor, gross motor, perceptual-motor, motor persistence, and cognitive competencies. They include novel devices we have developed (Continuous Performance Road Tracking task, Automated Sequencing task, Pinball task); subtests from the Wechsler Intelligence Scale for Children–Revised (Block Design, Mazes, Coding, and Similarities); and adaptations of other measures previously used in studies with children (Harcherik, Carbonari, and Cohen 1982). To assess "soft" or "minor" neurological signs, measures of motor impersistence, sequenced movements, laterality, and various gross motor tasks are used. Also included are RT measures, marble sorting tasks, and pegboard tasks; these are sensitive measures of fine motor or perceptual-motor maturity (Shaywitz, Cohen, and Shaywitz 1978; Harcherik et al. 1982).

Medical evaluation. Children with neuropsychiatric disorders may suffer from specific medical disorders that are etiologically related to their neuropsychiatric impairment. In addition, children with developmental disturbances may have other medical difficulties that have not been observed during the course of their standard medical care. Children involved in the Yale neuropsychiatric investigations routinely receive intensive medical evaluation. At times, this has led to interesting research observations. For example, we have found that many children with autism have elevated levels of blood lead, secondary to their mouthing of physical objects. Each child in the research protocols receives extensive laboratory screening of urine and blood samples. All children receive an electroencephalogram (EEG), with sleep deprivation when indicated, and computerized brain tomogram (ACTA scan). Additional biomedical evaluation is obtained, as indicated. For example, chromosomal studies are obtained on children with stigmata, including special banding techniques and culture for Fragile X syndrome which has recently led to the definition of a new biological subgroup of developmentally disabled and autistic children.

Specialists in pediatrics, human genetics, endocrinology, and neuro-ophthalmology provide further consultation.

School reports. Most children involved in the neuropsychiatric evaluations, except for the youngest children, are students in regular classrooms or special programs. Schools can provide rich descriptions of children's cognitive competence, since teachers have the opportunity to observe children for many hours daily and over many months. The Yale researchers are particularly fortunate in the close relationship between Yale and the major special schools and programs for developmentally disturbed children in the New Haven area. Senior Yale investigators are intimately involved as consultants with the major institutions serving the children in most of the protocols. The schools regularly provide investigators with detailed academic reports and progress notes; teachers also complete specialized forms, such as the Parent-Teacher Questionnaire, Childhood Personality Scale, Yale Child Behavior Rating, Yale School Report, and Tourette Syndrome List. Through detailed discussions with teachers and supervisors at the special programs, it is often possible to achieve greater certainty about the nature of a particular child's difficulties (e.g., in the, at times, difficult discrimination between autism and central language disorders, or in the specification of the nature of a child's attention difficulties).

Videotape recording. Videotape recording is a standard part of behavioral recording, supplementing and enriching the narrative account of a child's mental status and current behavior (e.g., in Tourette's syndrome); to assess inter-observer reliability in scoring behavior; to follow developmental changes and the impact of interventions such as medication; to review a series of patients during the process of data analysis (e.g., in developing rank orderings for a particular dimension of behavior); and to teach other clinicians about features of developmental psychopathology. All children in the research protocols are videotaped as part of their initial evaluation and then as indicated in specific protocols, often in standard situations: a simple interview with a familiar clinician; while engaged in a cognitive task (with an educator) at the child's usual level of academic achievement; and during a meal or snack. These three situations allow assessment of a child during interpersonal interaction, while confronted with structured cognitive material, and when allowed to function independently.

Inpatient observation. Children admitted to the Children's Clinical Research Center (CCRC) are intensively observed, providing rich behavioral information that extends data obtained from other sources. CCRC nurses are trained in behavioral observation and description, and are familiar with the range of neuropsychiatric disorders covered by the research protocols. The opportunity for intensive observation during inpatient evaluation may reveal unsuspected competencies (e.g., cognitive strategies in severely autistic children) or areas of difficulty (e.g., excessive anxiety about sleep or provocative behavior in children with attentional or tic syndromes).

Assessment of change. Behavioral assessment and rating instruments have only recently attained general use in child psychiatry, and are particularly inadequate in areas that clinicians would emphasize as most significant when evaluating a patient, i.e., predominant emotions and their determinants, interpersonal interactions, social involvement, and function at work or school (Rapoport 1978). Productive research will be impeded until scales for these psychosocial parameters are developed. While measurement of change in areas of individual function is a fundamental necessity for clinical research, it presents additional problems, particularly in relation to the difficulty in distinguishing among simultaneously operative sources of change and in adapting measures to the differing questions arising from short- or long-term observation periods.

Changes in the status of a child's disorder may simply indicate the process of development (e.g., the decrease in activity of attentionally disordered children moving into adolescence), reflect transient alterations in a child's world (e.g., the exacerbation of chronic, multiple tics with emotional tensions near a holiday), or show the effects of specific treatment interventions (e.g., educational programming, behavior modification, psychopharmacological agents, parent involvement, or psychotherapy). It is often difficult to separate these factors as determinants of change in a group of indices. To assess change, some of the individual scales described above can be administered several more times, generating a repeated measures design which adds to the value of the studies, particularly when they involve a small number of subjects. Yet, the requirements of individual studies frequently do not permit this solution, either because of the nature of the source of the change (as above), or because there are radical differences in the time frame involved. For example, some protocols examine change over long periods of time (such as studies of the natural history of a disorder or metabolic changes with development, requiring 5- to 10-year intervals), while others reflect changes occurring over a few hours (such as the neurochemical and neuroendocrine response to stress). Existing scales can be used to delineate change in clinical parameters (e.g., the Timed Behavioral Rating sheet developed by I. Cohen and M. Campbell for psychotic youngsters), but basic work in the development of new scales is critically necessary.

Neuropsychiatric Research in Childhood: Biological Measures

Because clinical biological studies are conducted without the opportunity to examine brain tissue directly, alternative strategies for coping with this limitation are required, including (1) studies on CSF metabolites of central amines, which provide the closest approximation of a sample of the biochemical function of the human brain now possible in the clinical situation, and (2) assessments of brain activity through measurement of each of the effector arms of the brain (the somatic muscular system, the autonomic nervous system, and the neuroendocrine system). While the somatic arm of the nervous system is invariably studied in psychiatry through behavioral measures and observations, attention to the other effector arms is more recent. The sympathetic nervous system (SNS) is a responsive indicator of "state" in behavioral studies, so that it is an especially informative measure in investigation of the impairments in the regulation of attention, arousal, anxiety, and general emotional state characteristic of many severely disturbed children. It can be monitored through a variety of psychophysiological indices (e.g., cardiovascular correlates) and through biochemical compounds associated with postganglionic neurotransmission. Biochemical investigation of SNS function is centered on the catecholamines, the postganglionic sympathetic neurotransmitter, and on compounds involved in their synthesis (e.g., dopamine-β-hydroxylase; DBH) and modulation (e.g., thyroid hormones).

The concept of the neuroendocrine system as an effector arm of the brain is derived from a convergence of evidence from clinical, morphological, and embryological studies (Pearse 1968; Mason 1975; Pearse 1977). Classical distinctions between the endocrine and nervous systems have been blurred as their common neuroectodermal origin and functional and morphological similarities have been clarified. Since cellular function in both systems typically involves secretion to external fluids and cells, the transport distance of a specific endocrine compound has been a basis for the distinction of the classical endocrine system (in which blood-borne hormones travel relatively long distances) from the nervous system (where the "local circuitry" of electrical and chemical information exchange may take place across the minute distances of opposed dendritic surfaces). From the vantage point of clinical neuroendocrinology, the distinction is not critical and the fullest examination of brain function includes the fluctuating activity of neuroendocrine systems. This triad of the effector arms of the brain (somatic-behavioral, autonomic, and neuroendocrine) is used as an organizing perspective in clinical biological studies.

Cerebrospinal Fluid Metabolites

Biogenic amine metabolism in the human brain can be studied by assay of CSF for the major metabolites of dopamine, serotonin, and norepinephrine (homovanillic acid, HVA; 5-hydroxyindoleacetic acid, 5-HIAA; and 3-methoxy-4-hydroxyphenethyleneglycol, MHPG, respectively) (Bowers 1972; Van Praag et al. 1975). The biogenic amine metabolites are excreted from the brain into the CSF, where their concentration is thought to reflect the state of the parent amines, or their turnover rate, in the brain. Diseases and medications alter CSF metabolite levels.

There are several methodological problems, including the need for lumbar puncture, differences between ventricular and lumbar CSF, possible moment-to-moment variability, and differences in contribution to CSF from various brain areas (Van Praag et al. 1973; Garelis, Young, and Sourkes 1974). Some of these problems have been overcome through the use of the probenecid method. For 10–12 hours before lumbar puncture, patients are given probenecid, a benzoic acid derivative which inhibits membrane transport and blocks the egress of the acid metabolites from the CSF. This produces increasing levels of these metabolites and a more accurate reflection of brain metabolism over a more representative period of time. We have determined the range of CSF metabolites in children with various neurological and neuropsychiatric disorders, such as autism, aphasia, cognitive processing disturbances, epilepsy, and nonautistic psychoses (Shaywitz, Cohen, and Bowers 1975; Cohen et al. 1980*b*).

CSF cannot be obtained for study from normal children. Instead, it has been necessary to contrast one diagnostic group with another and to use children suffering from various other conditions in which a lumbar puncture (LP) and examination of CSF are indicated (e.g., headache and disc disease). In our methodology, probenecid is administered orally in four divided doses over 10–12 hours, for a total dose of 125–150 mg/kg. A lumbar puncture is performed between 8:00 a.m. and 9:30 a.m., and the second or third 5 cc aliquot is immediately frozen for assay of metabolites and probenecid (Bowers 1972; Korf and Van Praag 1971; Cohen et al. 1974, 1977; Anderson, Young, and Cohen 1979; Anderson et al. 1981*b*). CSF is also examined for cells, protein, glucose, immunoglobulins, and folate.

Studies with adults indicate that membrane blockade becomes effective when a substantial amount of probenecid has been ingested (usually 100 mg/kg orally over 18 to 20 hours), or when CSF probenecid levels above 20 μg/ml have been achieved (Tamarkin, Goodwin, and Axelrod 1970). However, interpretation of metabolic data without actual measurement of CSF probenecid may be misleading because of the relationship between metabolite concentrations and CSF probenecid levels at lower CSF probenecid concentrations (Sjostrom 1972). In a study of 43 children, the levels of metabolites were highly correlated with the levels of probenecid achieved (Cohen et al. 1977).

Special methods of data transformation have been used to take into account the metabolite-probenecid relation. The amine metabolites may be statistically adjusted by analysis of covariance, or the metabolites may be expressed as a ratio to probenecid (nanograms of metabolite per micrograms of probenecid), which we designate as the HVA/P or 5-HIAA/P ratio (Cohen et al. 1974, 1977). The importance of measuring probenecid and relating the monoamine metabolites to the levels of probenecid achieved in the CSF has recently been reinforced by a report of observations similar to ours in adult patients (Berger et al. 1980).

Without probenecid loading, the concentrations of the two major metabolites of dopamine and serotonin (HVA and 5-HIAA) in autistic children are low, closely clustered, and within the range roughly defined for adults. Determined in six autistic boys (ages 6–15), HVA ranged from 45 to 100 ng/ml (mean ± SE = 65 ng/ml ± 7.7), and 5-HIAA ranged from 36 to 60 ng/ml (mean ± SE = 41.2 ng/ml ± 4.2). Following 10–12 hours of oral probenecid, the accumulations of amine metabolites increased significantly. The acid metabolites were correlated with the levels of probenecid achieved in the CSF. In a study of 34 other neuropsychiatrically impaired children using probenecid loading, the correlation between HVA and 5-HIAA was .57 ($p < .001$). The relation of each metabolite to CSF probenecid was statistically significant: probenecid and HVA, $r = .47$ ($p < .001$) and probenecid and 5-HIAA, $r = .50$ ($p < .001$). For this population of autistic and other neuropsychiatrically disabled children, the major difference between diagnostic groups was a reduced level of CSF 5-HIAA accumulation in the autistic children as compared to the age- and sex-comparable, nonautistic, early onset psychotic children (Cohen et al. 1977). This finding may be related to differences in the severity of the disorders, since the autistic children were more pervasively afflicted.

The functional relations between HVA and 5-HIAA may differ among diagnostic groups, reflecting differences in the balance between the parent neurotransmitter systems. To assess this relation, regression curves may be compared or a ratio of 5-HIAA/HVA may be constructed both for individuals (within a group) and for diagnostic groups. This ratio may be especially important in light of the different roles played by serotonergic and dopaminergic mechanisms in the organization of behavior. For example, the serotonergic midbrain raphe system may subserve sensory modulating or gating functions, while the dopaminergic system appears to be involved in motor activation and arousal (Singer et al. 1978). As will be discussed, the ratio of the metabolites of these two systems may be related to aspects of behavioral disorganization. Most studies of adult schizophrenia and depressed patients using the probenecid method have reported a ratio of 5-HIAA/HVA between .5 and .7. For autistic children, the 5-HIAA/HVA ratio is at the lower end of the adult range. This may reflect, in part, the relatively higher HVA levels observed during childhood and a negative relation between CSF dopamine metabolites and age.

CSF metabolite concentrations span a considerable range within the autistic and nonautistic early childhood psychosis groups, and the detection of between-group differences is difficult. Thus, we have used alternative strategies which (1) delineate subpopulations within diagnostic groups and (2) correlate metabolites with dimensions of behavior. In studies of childhood psychosis, we have scored dimensions such as language comprehension and expression, activity, movement abnormalities, and social relatedness, using rating scales completed by clinicians, parents, and teachers (Cohen et al. 1980*b*). One subgroup within the autistic population was found to have elevated levels of CSF HVA, both absolutely and in comparison with 5-HIAA (as reflected in 5-HIAA/HVA ratios). This subgroup was behaviorally distinguished by the greatest degree of stereotypic, repetitive behavior (flapping, twirling, finger flicking, and the like) and locomotor activity, and was overall the most severely afflicted group.

Correlations between CSF metabolites and ratings of behavioral dimensions, completed by clinicians familiar with all aspects of the child's history and condition and by other clinicians "blind" to everything but current behavior, have suggested hypotheses about serotonin and dopamine metabolites and the organizaiton of behavior. For example, for 10 autistic children, HVA/P was negatively correlated with behavioral ratings of social responsiveness and attention; the ratio of 5-HIAA/HVA was also highly correlated ($r = .97$, $p < .001$) with these behavioral ratings. Autistic children with higher competence had higher levels of 5-HIAA and lower levels of HVA in their CSF. For 33 neuropsychiatrically handicapped children, social responsiveness and attention were positively related to 5-HIAA ($r = .31$, $p = .08$) and 5-HIAA/log P ($r = .39$, $p = .03$). Thus increased serotonin turnover, as assessed by measurement of metabolite concentration following probenecid, was associated with a lesser degree of impairment in social and attentional functioning in autistic and neuropsychiatrically disturbed children. In recent studies with medical pediatric patients, repeated examinations of CSF without probenecid loading suggest that metabolite concentration may be a relatively stable, individual characteristic (S. MacIntosh et al., unpublished observations). The availability of reliable and sensitive HPLC methods for assaying metabolites and the use of various neuropharmacological approaches, in which CSF metabolites are the dependent variable, may reduce the need for probenecid loading for certain types of clinical studies. The use of probenecid provides the advantages described above; the investigation of CSF metabolites without probenecid will reduce the nausea and methodological difficulties related to probenecid. Continuing research will indicate which approach is best in a particular study.

While CSF MHPG levels cannot be determined in normal children, because of ethical constraints on performing a lumbar puncture, they might be measured in essentially normal contrast groups (children worked up for recurrent headaches, dizziness, etc., with no abnormal neurological or laboratory findings). When CSF MHPG levels of adult neuropsychiatric patients were used for comparison, the CSF MHPG levels of six medication-free autistic boys were normal. Recent data on pediatric medical patients have produced consistent findings, with MHPG ranging from 7 to 12 ng/ml. CSF MHPG measured in six children with Tourette's syndrome of chronic multiple tics (TS), each of whom either received probenecid loading or recently discontinued a medication, were distributed into two groups. Four patients were within the "normal" range, while two TS patients had increased CSF MHPG levels (near 15 ng/ml). The two patients with increased CSF MHPG levels suggest a subgroup of Tourette's syndrome patients with increased noradrenergic activity, perhaps responsive to treatment with agents which reduce central noradrenergic activity, such as clonidine (Young et al. 1981*b*).

The early-onset, pervasive behavioral disturbance and the high incidence of seizures and other neurological findings in children with autistic-like syndromes suggest that this syndrome might sometimes be caused by a congenital or early viral syndrome. Further support for this hypothesis is the high incidence of autistic-like syndromes in children with congenital rubella (Chess 1971; Fish and Ritvo 1979). CSF protein, immunoglobulins, and colloidal gold were measured in autistic children without neurological findings and were found to be normal (Young et al. 1977). Since this study, similar measures have been obtained in other children with primary and secondary autistic syndromes with negative results. The failure to detect abnormal CSF immunoglobulins does not rule out an etiological role for a slow-acting virus. However, the progressive improvement observed in some children with autism and the absence of other findings of CNS degeneration are unlike other disorders caused by slow virus infections.

Folate and vitamin B_{12} metabolism were examined in more than 60 children with childhood neuropsychiatric disorders, including 20 children with primary childhood autism. Folate in CSF, serum, and red blood cells, and B_{12} in serum, were normal in autistic patients, other neuropsychiatric patients, and normal controls. The findings also suggested that there is an active transport system regulating CSF folate independent of blood levels, except in cases of extreme folate deficiency (Lowe et al. 1981).

In summary, CSF metabolites in the serious, early-onset neuropsychiatric disorders of childhood show great variability within each diagnostic group, with no major differences between groups. However, there are relations between CSF metabolites and specific dimensions of behavioral impairment; in general, following probenecid administration, more disorganized children have relatively lower concentrations of CSF 5-HIAA and higher concentrations of CSF HVA.

Sympathetic Nervous System

Psychophysiological Measures. Difficulties in focusing and maintaining attention are found in a variety of psychiatric disturbances in children and adults (Silverman 1964; Mostofsky 1970). Attention, arousal, and unusual sensitivities have been particularly prominent theoretical issues in the study of children with early onset psychosis, such as childhood autism.

Detailed analyses of attentional processes in autistic and other severely disturbed children have been impeded by difficulties associated with the children's behavioral problems, such as hyperactivity and lack of cooperation. To assess arousal, attention, and perceptual processing, investigators have made use of a variety of nonverbal, physiological measures. These have included EEG, event-related potentials (ERP), and elicitation of vestibular nystagmus. Cardiovascular indices of psychophysiological processes have not been so intensively studied with children suffering from neuropsychiatric disturbances as they have in normal infants and adults.

In adults, heart rate, blood pressure, and respiratory rhythm have been used to assess general arousal and anxiety. Measures of peripheral blood flow are particularly sensitive for psychophysiological correlation with emotional and attentional states (Whitney 1953; Matthews and Lader 1971). Blood flow to muscles can be assessed by measuring the increase in the volume of an extremity when venous flow is occluded and arterial flow remains unimpeded (venous occlusion plethysmography). Using various plethysmographic methods, studies have demonstrated that threats, fear, imagined scenes, and a difficult mental task all may lead to vasodilation and increased muscle blood flow.

Peripheral blood flow changes may be associated with more specific aspects of attention (Williams et al. 1975). During tasks which elicit an external direction of attention, such as reading a blurred word on a screen, individuals show decreased forearm blood flow and increased resistance. With internal direction of attention (e.g., mental arithmetic) and sensory rejection, there is increased forearm blood flow and decreased resistance (Williams et al. 1975). These indices have been correlated with biochemical indices of catecholamine metabolism.

The sensory intake-sensory rejection hypothesis is quite relevant to children with disturbances of attention (such as in childhood autism). We have performed the first systematic studies of peripheral blood flow and resistance in normal and disturbed children during various attentional tasks (Cohen and Johnson 1977). Normal children responded like normal adults to attentional demands: increased flow with inner direction to attention and decreased flow with external direction of attention. Autistic children were markedly abnormal in two respects: their baseline levels of flow were significantly increased, and they failed to show task-related changes in their cardiovascular indices of attention (Kootz and Cohen 1981). These findings were interpreted as consistent with a persistent state of sensory rejection and increased arousal. When young adults were studied during two types of interviews (stressful and nonstressful) and various sensory intake and rejection tasks (Kootz, Gold, and Cohen 1979), the most salient parameter relating to cardiovascular indices was the degree of mental effort that was required, as hypothesized by Pribram and McGuinness (1975).

Autistic children who were higher functioning intellectually acquired a reaction time task, while lower functioning children failed to learn the task even after 25 practice sessions. The higher functioning children displayed the normal patten of cardiovascular correlates of external direction of attention (Kootz, Marinelli, and Cohen 1982); the lower functioning children did not. Autistic children as a group appear to be in a state of increased arousal and relative sensory rejection (see below). When they are able to acquire a task that requires attention to the external world, however, they show the normal accompaniment of cardiovascular correlates.

Several studies have been done to evaluate the cardiovascular correlates of attention in autistic children. In the first of these studies, 14 autistic children were compared with 16 controls during conditions of rest, social interaction, and a reaction time task. The autistic children had a significantly higher resting heart rate; the resting mean blood pressure was also elevated in the autistic group, but not to a significant degree. These findings suggest increased autonomic nervous system activity in autistic children. However, in the interview and reaction time situations, the autistic children did not display the significant changes in heart rate, mean blood pressure, peripheral blood flow, and peripheral vascular resistance that were seen in the normal control group. These findings are consistent with theories of a heightened state of sensory rejection in autism (Kootz and Cohen, in press).

A second series of experiments was designed to assess the hypothesis that autistic children prefer proximal (touch, taste) to distal (sight, hearing) sensory modalities. Autistic children were compared to control children by analyzing response times to auditory, visual, and tactile cues. Response times of the autistic children were significantly slower than those of the control subjects and were significantly related to mental age within the autistic subgroup. However, the autistic children had the same pattern of response as the normal children, responding most rapidly to auditory stimuli, followed by visual and tactile stimuli in that order. This suggests that autistic children's preference for proximal stimulation reflects a continuation of immature behavior, rather than a basic disturbance in sensory receptor sensitivity (Kootz, Marinelli, and Cohen 1981).

Blood and Urinary Indices. Various biochemical measures can be assessed as indices of sympathetic nervous system (SNS) function, including catecholamines, DBH activity, and thyroxine indices. Assessment of SNS activity by multiple techniques is particularly important in the childhood psychoses, since "vasovegetative" disturbances (presumably representing autonomic dysfunction) have been reported in clinical studies for many years.

Plasma and urinary catecholamines. Catecholamines are present in body fluids in very small quantities because of the processes of immediate reuptake and metabolism by monoamine oxidase (MAO) and catechol-*O*-methyltransferase (COMT); catecholamines in the plasma are measured in picogram per ml amounts and subject to rapid fluctuation. Older fluorometric assay methods did not achieve a level of sensitivity and accuracy sufficient for analyzing such clinical specimens as plasma and CSF. Radioenzymatic assays are now available which are less complicated but very sensitive and reliable, enabling the assay of a greater number of samples in a shorter period of time. An alternative method, which does not require the use of radioisotopes, couples ion exchange liquid chromatography (LC) and electrochemical detection (Hallman et al. 1978). We have established this LC method in our laboratory because of its reliability, efficiency, and sensitivity.

The measurement of plasma norepinephrine (NE) has been used as a method for the evaluation of normal sympathetic function; the increment in plasma NE (over basal levels) has been assessed while using such standard stresses of the SNS as postural change, exertion (isometric hand grip), and the cold pressor test. These indices have been applied to the investigation of patients with autonomic dysfunction, contributing to the delineation of subgroups of patients with primary orthostatic hypotension (Lake, Ziegler, and Kopin 1976; Ziegler, Lake, and Kopin 1977), and demonstrating the importance of age correction in comparative studies of plasma NE between normotensive and hypertensive groups (Ziegler, Lake, and Kopin 1976; Lake et al. 1977). The use of plasma NE as an index of sympathetic function rests on the assumption that the plasma levels are derived essentially from the postganglionic sympathetic nerve endings, while it is well known that NE is also secreted from the adrenal medulla (Louis, Doyle, and Anavekar 1973; Lake, Ziegler, and Kopin 1976; Taylor et al. 1978). It has been suggested that there is a differentiation in the functional source of NE because under normal physiological conditions the SNS is the major source of plasma NE, while, when there is a stress present, the adrenal contribution to plasma NE increases (Popper, Chiueh, and Kopin 1977). A careful study was performed in which the stress component was minimized while using conscious, unrestrained rats; although plasma NE does have a dual origin, at baseline levels of functioning the primary source of plasma NE was the sympathetic nerve endings (Micalizzi and Pale 1979). When there is an increase in plasma E levels, this seems to be an indication that the adrenal contribution to plasma NE levels has also increased and might no longer be an accurate index of SNS function (Peuler and Johnson 1977; Landsberg and Young 1978; Micalizzi and Pale 1979).

The marked responsiveness of plasma catecholamines to psychological and physical stimuli requires that blood collection procedures be meticulously standardized to minimize the effects of venipuncture, posture, and general environmental stimulation. Basal NE levels are obtained while the subject rests supine in a quiet room, at least 20 minutes after venipuncture. A standard assessment of the integrity and responsiveness of the SNS appears to be most satisfactorily achieved by obtaining the basal plasma NE level, then adding two additional increments of physical stress; sampling after standing for 5 minutes, followed by squeezing a hand dynamometer for 5 minutes at 30 percent of maximal effort. The tilt test, cold pressor test, and heavy work on a bicycle ergometer were not found to be so useful as the above strategy (Lake, Ziegler, and Kopin 1976; Kopin 1979).

Normetanephrine (NMN) is a major metabolite of NE and appears to reflect the degradation of newly synthesized and released NE; it is produced by *O*-methylation at a rate proportional to nerve stimulation, and is derived from both adrenal and peripheral sympathetic sites. Plasma NMN levels are 20–25 percent of plasma NE levels in man, and the two vary in parallel in response to suppression or activation of sympathetic nerve activity. The significant correlation of plasma NE and NMN indicates that plasma NMN levels can be used as an index of sympathetic function (Kobayashi et al. 1980).

A simple, sensitive, reliable method (using high performance liquid chromatography with fluorescent detection) is available for the determination of urinary dopamine (DA), norepinephrine (NE), and epinephrine (EPI) (Anderson et al. 1981*a*). This is of special value in pediatric research because venipuncture and the relatively large amount of blood required for serial catecholamine (CA) samples can be avoided when caring for small children. For example, in a study using urine samples collected over periods of only an hour or more, urinary CA levels were assessed in relation to performance measures in children and adolescents. In general, higher levels of CA excretion were associated with better performance in terms of speed, accuracy, and endurance. Similarly, in relation to enduring psychological characteristics, increased EPI excretion was associated with higher IQ and school achievement and greater "ego strength" and "emotional stability" (Frankenhaeuser 1975). These interesting studies require replication and extension.

Our initial studies of 24-hour urinary free catecholamines in autistic boys indicated significantly reduced levels in the group with severe cognitive and adaptive impairments. In more recent studies of urinary CA levels, we are examining DA, NE, and EPI separately, and using 1- to 8-hour collection periods in order to establish a procedure which will be more responsive to the short-term influences which the CA may be particularly well-suited to detect. Plasma catecholamines are being measured in challenge studies with clonidine and methylphenidate, as described below.

Plasma and urinary CA metabolites. Several research groups have studied brain NE metabolism in children by measurement of MHPG, the major metabolite of NE in the brain (Maas and Landis 1968; Schanberg et al. 1968), based on the possibility that levels of MHPG in body fluids would provide an index of noradrenergic activity (Korf, Aghajanian, and Roth 1973; Maas et al. 1977, 1979; Crawley et al. 1978; Crawley, Maas, and Roth 1979; DeMet and Halaris 1979).

Autistic boys have reduced 24-hour urinary MHPG levels when compared to same-aged normal boys also studied as inpatients (Young et al. 1979). Similar urinary volumes and creatinine excretion in the two groups indicate that the difficult urine collections from these children were complete. The reduction in MHPG excretion is not related to activity level, since most autistic patients were very active even while hospitalized.

Simultaneous measurement of free catecholamine excretion in these autistic children showed them also to be reduced in comparison to the control group (Young et al. 1978). The method for the determination of urinary free catecholamines measures NE and EPI, but not DA. Free NE accounts for 80–90 percent of the free catecholamines measured (Crout 1961). While free catecholamines are predominantly derived from peripheral noradrenergic activity, two points suggest that this measure could be useful in studies of infantile autism. First, disturbances in attention and arousal can be monitored through cardiovascular indices of sympathetic function and might be correlated with peripheral concentration of NE, the sympathetic neurotransmitter. Cardiovascular correlates are altered in autism (Cohen and Johnson 1977). Second, there is reason to expect a correspondence between urinary levels of free NE and MHPG because the locus ceruleus may exert a regulatory influence on peripheral sympathetic function through extensive pathways to the brainstem and spinal cord. In this sense, even peripherally derived MHPG is responsive to prevailing central noradrenergic activity (Crawley, Maas, and Roth 1980; Crawley, Roth, and Maas 1979).

The disordered regulatory mechanisms in autism (including repetitive stereotypic movements, rushes of anxiety, impaired attention and arousal, and hyperactivity in many children) led to the anticipation of increased noradrenergic function in autism. The unexpected reduction might reflect a developmental vulnerability or a response to persistent stress and anxiety, but its actual origin, and whether it is primary or secondary, needs further study (Young et al. 1978).

Although 24-hour urinary MHPG levels have not been measured in mentally retarded children, the levels in seven adults with Down syndrome were not different from levels in controls; 24-hour urinary HVA levels were significantly reduced in Down syndrome patients (Mann et al. 1980). These results suggest that urinary MHPG levels are not simply reduced in all severe neuropsychiatric disorders of childhood, but might be the basis for discrimination among some groups.

Plasma free MHPG levels of normal boys were within the "normal" range for adults. Autistic and TS patients who had not received any medication for a month or longer also had plasma MHPG levels in this range. However, among seven TS patients taking medication, two had increased plasma free MHPG levels; each had discontinued a medication active at the dopamine receptor 3 weeks before venipuncture (pimozide and haloperidol) (Young et al. 1981*b*). Elevated plasma free MHPG in these children might indicate a subgroup of TS patients with impaired noradrenergic function or might be drug induced. Increased plasma free MHPG levels in these patients could be related to an interaction of the NE and DA neuronal systems, secondary to a supersensitive DA receptor following withdrawal of an agent active at the receptor. In recent studies in our laboratory, baseline levels of plasma and urinary MHPG appear to be normal in TS.

A strong correlation between plasma free and urinary total MHPG levels measured simultaneously in eight normal boys suggests that noradrenergic function may be sufficiently stable to be reflected in both plasma and urinary measures (Young et al. 1981*b*). This is in contrast to the lack of correlation between plasma free MHPG and urinary total MHPG observed in nine adult psychiatric patients, although an "outlier" may have confounded this potential relation (Sweeney et al. 1980). In studies of normal adults, significant positive correlations between (1) plasma free or conjugated MHPG and CSF total MHPG (Jimerson et al. 1981) and (2) urinary total MHPG and CSF free MHPG (Maas et al. 1982)[1] indicate that there might be a correspondence among MHPG levels in the three body fluids. The small number of subjects in these studies, developmental changes in the pattern of NE secretion and metabolism, sampling inconsistency due to the secretion of free MHPG into the plasma in pulses (rather than continuously), the conversion of MHPG to VMA in the periphery (Blombery et al. 1980), and the underlying disease in the patient group are among the factors that might contribute to discrepancies. The number of patients with simultaneous MHPG determinations in two or three body fluids must be increased, and specific conditions affecting their relations studied, before the relations among these measures can be established.

Serum DBH. Dopamine-β-

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[1] Personal communication.

hydroxylase (DBH) catalyzes the conversion of DA to NE, and its release from sympathetic nerves is proportional to that of NE (Weinshilboum and Axelrod 1971). It has not proved to be the simple indicator of SNS activity first hoped for, and its clinical usefulness is now controversial. Animal studies have indicated that serum DBH is increased by such sympathetic stresses as forced immobilization, acute swim stress, or the cold pressor test (Lamprecht, Williams, and Kopin 1973; Wooten and Cardon 1973). Its sympathetic origin has been demonstrated by the lack of effect of adrenalectomy on serum levels, as contrasted to the reduction of serum DBH following destruction of sympathetic nerves with 6-hydroxydopamine or disease (Weinshilboum and Axelrod 1971; Noth and Mulrow 1976; Cubeddu et al. 1979). However, DBH is not sensitive to other stresses of the sympathetic system, the changes in DBH are quite small relative to the stress when it does elicit an increase, and there is no relationship between prevailing blood pressure and DBH (Goldstein et al. 1974). Although the enzyme is quite stable for an individual with repeated measures over a period of months, there is wide variation (in the range of 100–fold) in serum DBH activity among adults with apparently comparable and normal sympathetic function. Further difficulties in the interpretation of serum DBH activity concern a variety of technical problems in its measurement, such as the presence of endogenous inhibitors and difficulties with each of the several assays in use.

The broad range in serum DBH activity in the normal population reflects the strong genetic component influencing serum DBH activity (Weinshilboum et al. 1973), so that interpretation of measurements between groups must be cautious; repeated longitudinal measures of activity in the same individuals will provide helpful information. Serum DBH has been measured in a variety of medical illnesses, such as hypertension (Reid and Kopin 1974; Laduron 1975; Schanberg and Kirshner 1976), with conflicting results and disputed interpretations as to their meaning; it has also been measured in several psychiatric populations: affective states (Shopsin et al. 1972); psychotic states (Wise and Stein 1973); Down syndrome (Coleman et al. 1974); childhood autism (Goldstein et al. 1976; Lake, Ziegler, and Murphy 1977; Young et al. 1980), and hyperactivity syndrome (Rapoport, Quinn, and Lamprecht 1974).

It has been suggested that most DBH present in the serum is not the product of exocytotic release from sympathetic nerve terminals, but is derived from continuous "shedding" of membrane bound DBH. This hypothesis would fit the lack of correlation between sympathetic neuronal activity and serum DBH turnover, as well as the reduction in serum DBH activity following damage to the SNS (Grzanna and Coyle 1978). Obviously, it also represents a further challenge to our understanding of the significance of serum DBH activity, as it suggests serum DBH activity is not an index of SNS activity.

On the other hand, studies have indicated that CSF DBH more accurately reflects the synaptic release of DBH, and that CSF DBH and serum DBH are derived from different pools. For example, the expected changes in CSF DBH activity following treatment with phenoxybenzamine (an increase) and clonidine (a decrease) are not accompanied by a parallel alteration in plasma DBH activity. This suggests that CSF DBH activity may reflect central noradrenergic activity (Lerner, Dendel, and Major 1980). In a preliminary clinical examination of this possibility, low DBH activity in CSF was related to an elevation of a specific profile on the Minnesota Multiphasic Personality Inventory characterized by "a general distrust of people, a suspicious questioning of their motives, and a fear of emotional involvement with others in spite of an exaggerated need for attention" (Major et al. 1980, p. 309).

A dissociation between plasma NE concentration and plasma DBH activity in clinical studies emphasizes the difficulties encountered when attempting to use plasma DBH activity as an index of SNS function. Assessment of SNS function in Down syndrome subjects replicated the finding of reduced plasma DBH activity, but the plasma NE levels were significantly elevated (Lake et al. 1979).

In general, DBH has given way to the plasma catecholamines as a sensitive and reliable biochemical estimation of sympathetic activity. However, the longer half-life of DBH raises the possibility that it could reflect sympathetic activity in a manner different from the immediately responsive plasma catecholamines; for example, it might be hypothesized that plasma DBH mirrors the cumulative effect of a longer period of sympathetic activity and provides a measure complementary to that of the plasma catecholamines.

Sympathetic effects on the

cardiovascular system are under the influence of central mechanisms, so that to this degree serum DBH activity may reflect CNS function. Treatment directed toward CNS mechanisms, such as psychotherapy, has shown a beneficial effect on mean blood pressure which is accompanied by a reduction in serum DBH (Stone and DeLeo 1976).

Our initial studies of serum DBH activity have replicated the wide distribution of DBH activity in psychiatric patients and normal controls reported by others, determined its relation to age during childhood, indicated the relative levels in several diagnostic categories, demonstrated familial clustering, and indicated that it is not related to thyroid function in euthyroid psychiatric patients and controls (Young et al. 1980). These results are further evidence that findings in clinical studies using serum DBH activity must be interpreted conservatively until this measure is better characterized.

Thyroxine indices. The interaction between thyroid hormones and the SNS has long been apparent to clinicians. These observations have been complemented by research specifying points of metabolic relations. For example, we have reported a negative relationship between CSF HVA levels in psychotic children and serum thyroxine measured at the time of the lumbar puncture (Cohen et al. 1974). Thyroid hormone has profound effects on brain development and function, and its possible role in childhood psychoses was indicated by the clinical observation that triiodothyronine (T_3) has beneficial effects when administered to psychotic children (Sherwin, Flack, and Stokes 1958; Campbell and Fish 1974). The basis for the possible therapeutic effect of T_3 in severely disturbed children is not known, but several lines of evidence suggest that thyroid-catecholamine interactions might play a role. We have conducted investigations of thyroid hormone in autistic children (Cohen et al. 1980*c*), thyroid influences on enzymes related to catecholamine function (Young et al. 1982*a*, 1982*c*; Young, Kyprie, and Cohen 1982), and on age-related changes in serum thyroxine indices (Young et al. 1982*b*).

Neuroendocrine System

Conceptual Issues. The close relation of neuroendocrine regulatory centers in the hypothalamus to other brain areas makes this system ideally suited as an indicator of fluctuating brain activity. Fundamental physiological relations within and among these systems have now been established, so that pathological deviations in function are more readily identifiable.

While there has been technical and conceptual progress in neuroendocrinology, there has been corresponding amplification of the complexity of functional systems, and the means required for adequate investigation of specific components. For example, basal levels might be normal, while dynamic stimulation and suppression studies reveal impairment; dissociated neuroendocrine responses to apparently unitary phenomena, such as stress, require careful definition of experimental variables; unanticipated changes in hormone levels in a direction opposite to that expected reflect the impact of one hormonal system on another; attempts to clarify normal and abnormal neurotransmitter function through pharmacological intervention with neuroendocrine measures are confounded by multiple neurotransmitters affecting the same hypothalamic cellular system, and the same transmitters acting on multiple neuronal systems, in the hypothalamus and throughout the brain. Only precise, systematic investigations will clarify aspects of neuroendocrine function in normal and impaired children. Our overall strategy for neuroendocrine investigation reflects the awareness that a profile of neuroendocrine response to a specific stimulation gives a more informative picture of possible stress/endocrine associations.

Neuroendocrine and Neurochemical Challenge Tests. Clinical assessment of neuroendocrine function in individual patients is often accomplished by measurement of a body fluid hormone at a single time point, recognized as an essentially static evaluation technique. Standard challenge tests for evaluation of human endocrine function are well tested in clinical medicine. This "dynamic" approach uses specific stimulatory or inhibitory compounds to probe for altered responsiveness in a hormonal system. Specific examples are L–dopa, propranolol, and insulin tolerance tests of growth hormone and prolactin, thyrotropin releasing factor stimulation of thyroid-stimulating hormone, and metyrapone inhibition of adrenocorticosteroid compounds.

One weakness of some clinical tests is the nonphysiological level of stimulation or inhibition used. The pharmacological stimulation of a neuroendocrine system through doses hundreds or thousands of time greater than the physiological fluctuation of naturally occurring compounds limits the potential of the test to an absolute "present" or "absent" assessment of the overall competence of the system. Most classical tests give no indication of the system's responsiveness within the usual range of variation when reacting to typical physiologically activating events. In order to measure modulatory competence and thresholds of neuroendocrine response, a range of stimulus intensities must be incorporated into the dynamic tests. Contemporary studies of neuroendocrine mechanisms require less severe, graded stimuli, capable of defining response thresholds and charting stimulus intensity-response curves for each neuroendocrine axis.

Challenge tests can be conceptually organized in several ways. The usual framework has been categorization of the challenge by the postulated anatomical locus of its principal effect. This is often done by designation of the hypothalamic-pituitary-target organ axis which is affected by the challenge; e.g., challenge of the pituitary by thyrotropin-releasing hormone or challenge of extrahypothalamic brain areas by psychological stress (Brown and Seggie 1980). Organization of challenge tests according to the hypothesized cellular locus of action of a pharmacological probe refers to actions on processes related to neurotransmitter function at the synapse; e.g., neuropharmacologic actions principally affecting synthetic enzyme function, the reuptake process, or the postsynaptic receptor (Brown, Friend, and Chambers 1979).

A range of other strategies incorporating a challenge test exist; while clinical investigators typically use them in an overlapping fashion, it is useful to separate them on a conceptual basis (table 1).

The fundamental strategy is the use of one drug as a (hypothetical) probe of a single hypothalamic neurotransmitter system, monitoring it through a specific peripheral neuroendocrine compound. The use of this strategy in a research protocol is organized according to the stage of clinical investigation of the drug probe (Haskett and Rose 1981). Initially, the challenge represents a simple clinical test of postulated neurochemical pathophysiology in a disorder (e.g., probing noradrenergic effects on the pituitary adrenal axis with amphetamine) (Sachar et al. 1981) or the attempted replication of findings anecdotally reported. If open tests merit continuing interest, the same challenge strategy is embedded in a rigorous research design which will determine the critical features and applicability of the drug probe. This standardization and validation of the drug challenge includes specification of its sensitivity ("true positives": the percentage of persons with the specific disorder who are correctly identified by a positive challenge test result) and specificity (the percentage of persons not affected with the specific disorder who are correctly identified by a negative challenge test result, the remainder indicating the "false positives"). The "predictive value" or "diagnostic confidence" is the critical variable when a test is used for diagnostic purposes, and indicates the percentage of total abnormal test results that are associated with (true positive for) the index illness (Vecchio 1966; Galen and Gambino 1975; Akiskal et al. 1979; Carroll et al. 1981). The final stage of the

Table 1. Clinical strategies for pharmacological challenge of neurochemical and neuroendocrine function

1. One drug, one neurotransmitter, and one neuroendocrine index
   a. Simple test of hypothesized neurochemical pathophysiology in a disorder
   b. Determination of clinical discrimination and utility: Standardization and validation of a drug probe
2. Several drugs affecting the same neurotransmitter, measuring a single neuroendocrine response index
3. Several drugs, each affecting a different neurotransmitter; i.e., several neurotransmitter effects on a single neuroendocrine response index
4. Several drugs affecting the same neurotransmitter, measuring several neuroendocrine response indices
5. One disease, multiple drug challenge tests
6. Drug used to reproduce the illness and its neuroendocrine abnormalities
7. Drug used to correct a neuroendocrine or neurochemical abnormality in a syndrome
8. Drug used to demonstrate genetic differences through a single neurochemical or neuroendocrine index

clinical application of a challenge test is its cautious extension to questions regarding natural history, treatment, and prognosis (Haskett and Rose 1981).

When possible pathophysiological mechanisms are considered, it is obvious that a single neurotransmitter neuronal system can be probed by several drugs (each affecting different features within the sequence of synaptic transmission) yet monitored through the same neuroendocrine index. For example, drugs such as clonidine, desipramine, amphetamine, and insulin have effects on the noradrenergic regulation of growth hormone release. A modification of this strategy is to choose a range of drugs which affect different neurotransmitter systems, but monitor the physiological effects through a single neuroendocrine response index. An example of this approach is challenging the hypothalamic-pituitary-adrenal axis with dexamethasone, amphetamine, and physostigmine, or probing growth hormone release with insulin, arginine, L-dopa, and clonidine. Finally, several drugs with specific effects on a single neurotransmitter system might be chosen, and the response monitored through measurement of several neuroendocrine response indices. For example, the effects of clonidine, desipramine, amphetamine, and methylphenidate on the noradrenergic system can be examined through measures of plasma cortisol, growth hormone, and luteinizing hormone.

Specific pharmacological challenge strategies are typically an intrinsic part of a more general plan for investigating a target disease through a series of drug challenges. A pattern of responses may indicate features of the underlying pathophysiology, or several challenge tests may improve on existing diagnostic procedures. This may be the case, for instance, when the dexamethasone suppression test, plasma cortisol response to *d*-amphetamine, cortisol secretory patterns, sleep studies, and the thyroid-stimulating hormone response to thyrotropin-releasing hormone administration are all considered in research studies of affective disorders.

Another type of challenge test strategy focuses on the reproduction of the symptoms of a disease and components of its physiological abnormalities. While such a strategy is usually not possible in the sense of preplanned administration of a drug which will elicit or aggravate symptoms of an illness, the clinician can utilize observations on patients who have administered drugs to themselves (e.g., psychotomimetics; Bowers 1977). Similarly, a pharmacological challenge is sometimes given to an unaffected relative of a patient with a known genetic disease in order to estimate the likelihood of the onset of symptoms at a later date for the relative (e.g., L-dopa in Huntington's disease). A more common strategy is to choose a drug which will correct a neurochemical or neuroendocrine abnormality in a sydrome, with the hope that it will also reduce symptoms as well; an example is the administration of clonidine in Tourette's syndrome, first attempted in order to reduce the apparently increased noradrenergic function in a subgroup of these patients.

Finally, a drug challenge test can be administered to multiple members of each of several families in order to determine if genetic patterns of response exist, and in what way they may or may not be related to a clinical disorder.

Clonidine and Methylphenidate Challenge Tests. We have designed challenge tests which are integrally related to central clinical questions. Challenge tests are administered initially in a baseline, pretreatment condition, followed by further challenges at subsequent posttreatment intervals judged to be appropriate on a clinical basis; changes in the metabolic response are examined in the light of clinical change. Placebo-controlled, double-blind designs are used after initial open trials. Metabolic responses are examined in responder and nonresponder groups as a possible key to discriminating them and identifying the physiological basis for their response.

Clonidine is a partial noradrenergic agonist which, when administered in low doses, preferentially acts at the afferent input to the principal nucleus of noradrenergic cell bodies in the brain, the locus ceruleus. Low doses of clonidine reduce the firing rate of neurons in the locus ceruleus and the production of MHPG in brain by selective activation of presynaptic alpha$_2$ receptors (Anden et al. 1970; Svensson, Bunney, and Aghajanian 1975; Cedarbaum and Aghajanian 1977). Elevated CSF free MHPG in a TS patient suggested a subgroup of TS patients with increased noradrenergic activity which might be responsive to an agent which reduces brain noradrenergic activity (Cohen et al. 1979*a*). An open trial of clonidine indicated that it achieves substantial symptom reduction in approximately 50–70 percent of TS patients (Cohen et al. 1979*b*, 1980*a*).

In our initial open studies, CSF free MHPG was measured in a single patient before and after a challenge dose of clonidine. His baseline level of 14.8 ng/ml was reduced to 10.4 ng/ml free MHPG after 1 month of clonidine treatment, accompanied by a good clinical response (Young et al. 1981*a*).

Three TS patients, unmedicated for at least 1 month, were given challenge doses of medication, and plasma free MHPG levels were obtained at baseline and 2 and 22 hours following medication administration. A 25–40 percent reduction in plasma free MHPG was observed following a challenge dose of clonidine (two severely disturbed patients) or haloperidol (a single patient with mild symptoms). All three patients had a good clinical response when treated with the challenge medication. Plasma free MHPG has not yet been measured in a medication-free nonresponder (Young et al. 1981*a*).

Challenge doses of clonidine given while a (responder) patient is on a maintenance dose indicate that a metabolic response can still be achieved. Plasma free MHPG, which had been very high at baseline in one patient, was reduced in the two postclonidine samples. The other responder given a clonidine challenge dose (while on a maintenance dose) had a 40 percent increase in plasma free MHPG at the 2-hour postclonidine point, before it was eventually reduced below baseline at 22 hours. One patient, who did not have a good clinical response while on maintenance clonidine, also did not have a decrease in plasma free MHPG following clonidine challenge (Young et al. 1981*a*). Further studies of clinical nonresponders will help clarify the relation between plasma free MHPG and clinical response to clonidine.

The use of other medications at the time of a clonidine trial tends to obscure plasma free MHPG changes. For example, while plasma MHPG might decrease during haloperidol treatment, it might increase during acute withdrawal from haloperidol.

A trial of clonidine was also attempted for two adolescent girls and one young adult man with infantile autism and led to a slight aggravation of their symptoms. Clonidine challenge produced a 40 percent increase in plasma free MHPG in the autistic girl in whom it was measured (Young et al. 1981*a*).

In recent protocols we have used clonidine and methylphenidate as pharmacological challenges to CA function in TS patients and attention deficit disorder while monitoring a greater range of variables. For example, we have designed the clonidine challenge test in TS to include blood pressure and sedation measures on the clinical side, as well as plasma clonidine, MHPG, HVA, and human growth hormone on the metabolic side.

Changes in MHPG levels following clonidine were accompanied by effects on behavior, altered levels of other metabolites, and a selective neuroendocrine response; the various effects are not simultaneous and vary in magnitude. The marked increase of growth hormone following clonidine (Lal et al. 1975; Gil-Ad, Topper, and Laron 1979) is a more robust, acute response than the plasma MHPG change (Leckman et al. 1980; Leckman, Maas, and Heninger 1981; Young et al. 1981*a*), suggesting that clonidine might have clinical application as a growth hormone stimulation test and that growth hormone response might be a sensitive test of brain function in some neuropsychiatric disorders. In a more basic way, the discrete effects of clonidine on specific clinical parameters (blood pressure, sedation, motor regulation) reflect the distinct action of clonidine on specific noradrenergic neuronal subsystems (e.g., hypothalamic, brainstem), in relation to the more general noradrenergic effect presumably reflected in MHPG levels. Since these effects are neither simultaneous nor of the same magnitude, evaluation of other regulatory influences (such as dopaminergic or serotonergic effects) will help to dissect components of critical control mechanisms acting on individual parameters.

An example of the initial direction of such studies is a comparison of plasma MHPG and HVA levels before and after a 12-week trial of clonidine in six TS patients. There were significant increases after 12 weeks of clonidine in the baseline morning levels of both plasma MHPG (15 percent increase) and plasma HVA (77 percent increase) (Leckman et al. 1982). While the specific physiological mechanism underlying these metabolic changes will require extensive investigation, the data suggest an interaction between the noradrenergic and dopaminergic systems in these patients. This interaction may mediate an increase in central DA turnover from the apparently low baseline turnover found in TS (Cohen et al. 1978*b*, 1979*a*; Leckman et al. 1982).

Using a similar strategy in protocols evaluating boys with attention deficit disorder, we have been able to examine the pharmacokinetics of methylphenidate (MPH), demonstrate dose effects on plasma MPH levels and a relation between plasma MPH concentration and clinical response, and indicate the rise in plasma human growth hormone and decline in plasma prolactin following MPH administration (Shaywitz et al., in press *a*). The large number of children taking stimulant medications, and the questions surrounding their long-term efficacy, make it mandatory that carefully designed, discretely targeted clinical and metabolic studies such as these be continued if we are to use stimulant medications knowledgeably. While there is a growing base of information concerning the attention deficit disorders and their treatment with stimulants (Shaywitz et al., in press *b*; Shaywitz and Shaywitz 1982), further application of the challenge test strategy promises an improved understanding of biological influences which will lead to optimal clinical care or to troubling side effects (Young 1981; Lowe et al. 1982).

The Development of Monoamine Neuronal Systems During Childhood

Normal Ontogeny. Another perspective in neurochemical research relevant to autism is examination of the development of functional balance of neurotransmitter neuronal systems in childhood and adolescence. Concepts guiding these studies are that (1) while levels of a compound in a fluid may be within the normal range established for adults, they may be unusual for a given period in childhood because of developmental changes; and (2) while levels of a compound may appear to be within a normal range for that age, an abnormal developmental profile of neuronal systems in a specific diagnostic group may be most visible when the relative functional interaction among systems is examined and found to be atypical compared to contrast and normal groups. Biochemical studies of childhood autism have required establishment of normal ontogeny of neurotransmitter neuronal systems through a composite assessment of transmitters, enzymes, and metabolites in body fluids in relation to age, and the delineation of overall functional relations among these systems (Young et al., in press).

Examination of maturational changes in biogenic amines, their metabolites, and related synthetic and degradative enzymes has suggested consistent developmental effects on aminergic neuronal systems. While dopaminergic activity appears to decrease over the period of childhood and adolescence, noradrenergic function appears to increase, and there is stable or decreasing serotonergic activity. These age-related changes may have fundamental behavioral effects. Increased dopaminergic activity leads to increased locomotor activity and stereotypic movements, effects modulated by relative levels of both noradrenergic and serotonergic activity. The apparent developmental reduction in dopaminergic activity parallels the decrease in motor activity as a child matures. Imbalance among monoamine systems, due to differences in developmental rates, might critically affect a child's behavior (Young et al., in press). Developmental changes in neuromodulators, such as hormones, might also be important determinants of behaviors associated with neuronal maturation (McEwen 1976).

Pathology of Neurotransmitter Ontogeny. As profiles of neurotransmitter maturation in various tissues and body fluids are established with more assurance, it will be possible to investigate the relation of abnormal developmental sequences at the molecular level to familiar clinical pathology. Pilot work along these lines is just beginning.

Sex Differences. As with age effects, there has been little systematic investigation of differences in monoamine function between males and females. Such studies may be of importance in understanding the difference between boys and girls in the incidence of certain types of disorders. For example, attention deficit syndrome, Tourette's syndrome, and childhood autism are three- or four-fold more common among boys. In neuropsychiatrically impaired children, we found a considerably higher dopamine turnover rate in boys than in girls. This difference did not appear to be related to diagnostic clustering of the boys and girls in different neuropsychiatric subgroups.

We have analyzed CSF sex effects in a larger population of patients, ages 3–20 years. In this child and adolescent population, the mean CSF HVA, following probenecid, for males ($n = 49$) was 204 ng/ml; for females ($n = 22$), HVA was 164 ng/ml. The HVA/probenecid ratio was strikingly higher in the boys (15.7) than in the girls (9.5, $p < .01$). Diagnostic differences between the boys and the girls must be considered in evaluating the meaning of the increased HVA and HVA/probenecid measures in males. Also, since the females tended to be older, the age effects noted in the previous section may account, at least in part for observed differences between the sexes (Leckman et al. 1980).

Clearly, considerably more research will be required to assess the relations of age and sex to monoamine neuronal systems and the implication of any trends for psychopathology. Age effects may clarify vulnerable periods for the emergence of psychiatric disorders (e.g., adolescence); also, there may be important interactions among neurochemical development, endocrinological maturation, and the onset or exacerbation of behavioral disturbances at periods of biological upheaval (such as moodiness at the transition into adolescence or the marked increase in aggression among autistic children at this phase of development) (Fish 1977).

Laboratory and Clinical Research: Treatment of Tourette's Syndrome With Clonidine

The syndrome of chronic, multiple tics described by Gilles de la Tourette consists of multiform motor and phonic tics and compulsive actions originating in childhood and persisting for years (Gilles de la Tourette 1885; Woodrow 1974). The initial hypothesis that this was a biologically mediated syndrome was later displaced by psychoanalytic theories postulating a predominantly psychogenic origin, based upon many observations of the precipitation or aggravation of symptoms by psychological stress. The subsequent use of haloperidol as a specific pharmacological treatment, coupled with the emergence of more sophisticated laboratory techniques, resulted in renewed biological research on Tourette's syndrome. Catecholamine metabolism was further implicated in the etiology of the illness by exacerbations produced by dopaminergic agonists, such as dextroamphetamine (Feinberg and Carroll 1979). Another line of evidence for a neurological substrate was the high incidence (40 percent in our series) of patients with abnormal or borderline EEGs. Abnormal findings related to maintenance of posture or to performance of sequential movements are found in 50 percent of patients; a similar percentage have cognitive processing disturbances (Shapiro et al. 1973; Harcherik et al. 1982).

Genetic mechanisms were suggested in the original paper by Gilles de la Tourette, who described a marked preponderance of males and possible familial clustering of the disorder. These observations have been replicated repeatedly, with most authors finding 3 to 8 times more male than female Tourette's syndrome (TS) patients. More sophisticated genetic studies support a strong genetic component, with simple and chronic multiple tics representing, in families with TS probands, an expression of the underlying vulnerability (Kidd, Prusoff, and Cohen 1980; Pauls et al. 1981).

Central nervous system metabolism in children with Tourette's syndrome has been assessed by measuring the cerebrospinal fluid metabolites of dopamine (HVA) and serotonin (5-HIAA) with and without the administration of probenecid. These studies revealed a reduced accumulation of CSF HVA and 5-HIAA, which may represent a primary decrease in the brain turnover of the parent compounds or a long-term adaptation to overactivity in these systems as a result of changes in receptor sensitivity (Cohen et al. 1978*b*).

The involvement of noradrenergic mechanisms in TS was suggested by (1) elevated MHPG in the CSF of a severely disabled child (Cohen et al. 1979*a*), (2) exacerbation of the syndrome by stress and anxiety, and (3) similarities between the clinical phenomena and some aspects of behavior elicited in animals by stimulation of the brain center which regulates noradrenergic activity, the locus ceruleus (Cohen et al. 1979*a*). A separate line of research in other laboratories at Yale used single cell recording techniques to investigate the neuropharmacology of the locus ceruleus, and the mode of action of clonidine, an imidazoline derivative used in the treatment of hypertension (Svensson, Bunney, and Aghajanian 1975). Clonidine is a partial adrenergic agonist. However, at low doses, it diminishes central noradrenergic activity by stimulating inhibitory presynaptic, α-adrenergic autoreceptors on neurons which regulate the locus ceruleus. For example, in a clinical application, clonidine has been found to suppress dramatically the noradrenergically mediated symptoms of methadone withdrawal in adults (Gold, Redmond, and Kleber 1978; Gold et al. 1980) and, as shown by our recent research, also in infants (Hoder et al. 1981).

The elevated spinal fluid MHPG in a child with TS, coupled with these basic and clinical studies of clonidine, suggested assessment of the usefulness of clonidine for TS. We have administered clonidine to 50 patients over the last 3 years. All were individuals who had not responded to haloperidol, had developed tolerance, or had discontinued it because of side effects. In our experience, 50–70 percent of patients have shown improvements in behavioral symptoms and tics, with no serious problems with side effects or tolerance (Cohen et al. 1979*b*, 1980*a*; Leckman, Detlor, and Cohen, in press; Leckman et al., in press).

Clonidine's ameliorative action on the symptoms of TS provides a gratifying example of the movement of data and hypotheses from basic science laboratories to the clinic, a course explicitly fostered by the organization of research within a university. Coordination of hypotheses and experimental results across laboratories, and the development of complementary strategies among investigators, play a critical role in generating research with relatively early clinical application.

This process was aided in TS by the relative specificity of the symptoms, the biochemical measures, and the psychopharmacological agent. By analogy, it might be predicted that advances in understanding childhood neuropsychiatric disorders will be based on careful diagnostic criteria, specific behavioral dimensions, and precise biological theories and techniques. At all phases of the research, animal studies are needed to clarify points that cannot be investigated in humans. This model for collaborative research offers the maximal opportunity for clarification of fundamental physiology and pathology, and successful application in treatment for children.

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Strategies for Study of the Neurochemistry of Attention Deficit Disorder in Children

by Robert D. Hunt, Donald J. Cohen, Sally E. Shaywitz, and Bennett A. Shaywitz

Abstract

The interpretation of neurochemical studies of attention deficit disorder (ADD) with hyperactivity is complicated by the variability in diagnosis and by the limitations of single neurochemical measures—whose levels may be compensated by chronic feedback mechanisms. This article reviews previous neurochemical studies of ADD and proposes the use of single-dose neurochemical probes. Administration of a provocative agent with subsequent sequential measures of plasma levels of neurotransmitters, their metabolites, and hormones may help define the responsivity of neurochemical systems. Blood levels of drugs and neurotransmitters following single doses of methylphenidate and clonidine are studied as a strategy to explore the responsivity of dopaminergic and noradrenergic mechanisms in ADD.

The ability to sustain and shift attentional focus is a major component of cognitive and emotional maturation. Many disciplines have pursued an understanding of the psychological and neurophysiological mechanisms of attentional and cognitive processes. Yet considerable ambiguity remains about the nature of attention and the neuronal mechanisms that underlie a child's ability to focus and shift his thoughts and orientation.

There is no single measure—behavioral, cognitive, physiological, or chemical—that uniquely spans the breadth of, or is adequately diagnostic of, attentional processes. Lacking a unique or sufficient marker or correlate of these processes, investigators sample a variety of phenomena along the attentional path. Perception, discrimination, and visual-motor integration are all components of a system that rapidly links internal and external events with behavioral output. Physiological measures of central nervous system (CNS) evoked response or of peripheral response to an orienting stimulus (e.g., heart rate, peripheral vascular resistance, and skin conductance) provide inferences about the processes of attention and arousal. Yet, no measure stands independently as a barometer of the multiple and simultaneous events that comprise attention. Investigators seek neurochemical and neurophysiological threads that will link the clinical behavior of a child restlessly gazing about the classroom to his performance on laboratory tests of sensory discrimination, reaction time, vigilance, and memory.

Selective neurochemical measures and neuropharmacological responses suggest some neurotransmitter components of attentional processes. Interpretation of individual chemical measures, however, is clouded by the imprecise relationship between the state or trait status of selected measures (e.g., enzymes, neurotransmitters, and hormones), *and* the cognitive or behavioral processes with which they may correlate. Furthermore, given the nervous system's ability to alter the sensitivity of chemoreceptors to their neurotransmitters, individual chemical levels cannot easily be interpreted without assessment of their receptor sensitivity. A growing litera-

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ture assigns significance to catecholaminergic mediation of information processing and the modulation of arousal, attention, and activity. The pursuit of these leads with more refined cognitive tasks, and more precise pharmacological probes, may illuminate mechanisms of the development and disturbance of attention.

Attention Deficit Disorder—Clinical Constellation and Diagnostic Considerations

The diagnostic criteria for attention deficit disorder (ADD) with hyperactivity as defined in *DSM-III* (American Psychiatric Association 1980) include the constellation of *hyperactivity* (running, climbing, fidgeting, and difficulties in staying seated or still); *inattention* (characterized by failing to finish tasks, not listening, easy distractibility, difficulty concentrating on school work or staying with a play activity); and *impulsivity* (including a tendency to act before thinking, to shift activities rapidly and to be disorganized in work or to require supervision). These symptoms can be considered indicative of ADD only if they appear before age 7 and persist for longer than 6 months. A primary diagnosis of ADD is not applied to the cognitive disturbances which occur within pervasive developmental disorder, schizophrenia, or manic-depressive disorder. But there are complex diagnostic and nosological connections between the symptoms of ADD and other neuropsychiatric conditions, such as Tourette's syndrome or borderline personality disorders (Cohen et al., in press).

The phenotypic expression of the attention deficit disorder (American Psychiatric Association 1980) changes with development. Careful history may disclose that the ADD child was an unusual infant. He cried a lot, was irritable, and slept less than most infants. He did not sustain play or exploration with one toy or object. He destroyed and lost even the most "childproof" toy. He wore out his clothes, his toys, and his mother's patience earlier than most toddlers. Many of these children are identifiable before they enter school because of their difficulty in modulating attention, aggression, and excitement. Their monitoring of internal stimuli and feelings may be as impaired as their difficulties in sustaining external attention (Cantwell 1975*a*; Millichap 1975; Cohen 1977; Lazor and Chandler 1978; Weiss and Hectman 1979).

By elementary school, these children frequently exhibit learning difficulties. Some appear to have primary perceptual problems, such as enhanced tendency to reverse letters and numbers. Others have reading difficulties (dyslexia), perhaps secondary to the impulsivity of their visual scanning. Learning difficulties also may reflect impairment in other aspects of cognition. For example, the correct sequencing of information or the discrimination of a relevant pattern or concept often requires sustained focusing on subtle aspects of a stimulus, subject, or thought. The impulsive child may miss sequences and patterns through repeated distraction. Similarly, the abstract or idiomatic meaning of a word which is partially defined by its context may be lost to the child who processes information in rapidly shifting fragments.

A specific learning disability exists when cognitive functioning in one modality or skill is impaired relative to other more general intellectual abilities. Many children with ADD may have specific reading or arithmetic disabilities (Clemmens and Kenny 1972; Gittelman-Klein and Klein 1976; Harris 1976; Rosenbloom 1972).

Attentional dysfunction frequently includes an insensitivity to social cues. ADD children often ignore facial expressions, are unaware of danger, and fail to anticipate the effect their behavior will have on others. Social difficulties reflect the impetuousness with which they approach relationships. Attentionally impaired children may have difficulty integrating discrepant cues from different sensory modalities and hence miss subtle discrepancies between what is said and what is implied (Whalen et al. 1979). ADD children try to intrude into and take over groups, and they may insist on being the leader. They often have little capacity for fairness, reciprocity, and taking turns. Recess provides too many opportunities for fights as the children bully or are bullied. ADD children may initially appear to be friendly, but they lose friends as quickly as they are made.

Frequently these children have a delay in development of fine and gross motor coordination, causing them to appear slow and awkward. Handwriting is usually sloppy; gross motor coordination is often floppy, loose, or disheveled. In spite of their bravado and provocation, these children frequently are poor athletes. Boys, probably because of their high activity level, are much more likely to manifest the behavioral and motoric components of this disorder (Shaffer 1978; Shaywitz 1982). Some attentionally impaired children are fidgety and impulsive; others are slow but competent in information intake and visual motor performance, and appear grossly hypoactive. Thus, ADD often occurs in association with other difficulties in modulation, including motoric hyperactivity, learning or cognitive disability, and poor social adjustment (Loney, Langbourne, and Paternite 1978; Loney et al. 1978).

By middle childhood, attentionally impaired children are often enmeshed in conflict. Parents are unable to "make them mind," teachers have difficulty making them learn and behave in class; peers are annoyed by immature, attention-seeking behavior; neighbors may complain of their negligence, destruction of property, or "bad influence" on other children. By middle childhood, symptoms of depression and low self-esteem may complicate adaptation. Failure to channel efforts into a meaningful sequence of accomplishments often leads children to achievement levels below their abilities and a lack of gratification and pride (Das, Leong, and Williams 1978; Huessy, Metoyer, and Townsend 1974).

Attentional deficit and impulsivity may persist into adulthood, although the motoric hyperactivity usually diminishes to manageable levels of restlessness. While some outgrow the effects of ADD, others have severe impulsivity and other difficulties as adults. They may develop personality disorders or have substantial antisocial and legal difficulties. ADD may be a precursor to some later forms of major affective disorder or psychosis (Mendelson, Johnson, and Stewart 1971; Minde, Weiss, and Mendelson 1972; Huessy, Metoyer, and Townsend 1974; Cantwell 1975*a*; Quinn and Rapoport 1975; Wood et al. 1976; Lerer and Lerer 1977; Hopkins et al. 1979).

Environmental Influence. Attention provides continuity of the linkage of a child's inner life to his external environment. The child's development of the capacity for sustained attention is enhanced by interaction with calm and predictable parents. An environment in which affection and rules are reliably provided allows safety for a child to direct his attention to his "work" of practicing and exploration. A chaotic family, prone to explosiveness and disaster, creates an endless whirl of distraction requiring the child's continued vigilance or worry. The child may not be able to focus energy into persistent pursuit of a goal (Sandburg, Rutter, and Taylor 1978; Rollins and Thomas 1979). Children from chaotic home environments may fail to develop the continuity of focus and the reinforced pursuit of meaningful goals which sustain investment of intellect and emotion.

Transient variations in level of the child's arousal, alertness, and motivation (his experience of the rewards and incentives for focusing on a task) all may alter attentional functioning. Clinical disturbances of attentional mechanisms may result from internal psychological conflicts which lead to preoccupation and an inward shift of attention. Attention may be diffused by a highly distracting environment or by anxiety about performance of a difficult academic task. Attentional deficit and hyperactivity may be specific to a particular task or setting for some children (Ellis et al. 1974; Barkley and Jackson 1977). Klein and Gittelman-Klein (1975) found that of 155 subjects who were hyperactive in the classroom, only 25 percent were hyperactive at home.

Attentional disturbance is a frequent component of more pervasive disorders such as autism, atypical development, and Tourette's syndrome (Cohen 1980; Jagger et al. 1982). In some cases, this attentional deficit may reflect a disturbance in attributing meaning to stimuli, or as shown by recent data, disturbances in physiological mechanisms that modulate arousal and intake of external stimuli in developmentally delayed children (Kootz and Cohen 1981).

Given the diversity of children whose attentional disturbance reflects a disruptive environment or a more global impairment of intelligence or personality, it is difficult to find a homogeneous population in which attentional disruption appears as a primary trait. Yet, the quest for clinical homogeneity, both as a behavioral pattern and a personality type, must precede and complement exploration of a common biological substrate.

Familial and Genetic Studies of ADD

Familial studies suggest a genetic contribution to the development of this disorder. The presence and severity of ADD in a specific child may reflect a response to either genetic vulnerability or environmental chaos and emotional deprivation. Clinical observations suggest that parents of hyperactive children have an increased prevalence of mixed psychopathology (schizophrenia, affective disorders, and sociopathy) (Wender 1971) and a greater incidence of neurosis, antisocial behavior, "nervous breakdown," suicide, and alcoholism (Satterfield et al. 1973). Stewart et al. (1966) found that more than half of 37 hyperactive children had a first or second degree relative with serious legal, psychiatric, or employment difficulties. Heavy drinking was associated with behavioral difficulties in 22 percent of the fathers and 4 percent of the mothers. A history of learning difficulties was evident in nearly a fourth of fathers and 10 percent of mothers of 83 hyperactive children (Mendelson, Johnson, and Stewart 1971).

In a more systematic psychiatric examination of the parents of 50 hyperactive children and 50 matched controls, Cantwell (1975) found that nearly half of the parents of hyperactive children met clinical criteria for diagnosis of a psychiatric disorder; this was in marked contrast to the virtual absence of psychiatric diagnoses in parents of controls. The main psychiatric diagnoses found in the parents of hyperactive children were alcoholism and sociopathy among fathers, and hysteria among both parents. Sixteen percent of the fathers of hyperactive children gave a history of having been hyperactive themselves, as children. This subgroup of previously hyperactive fathers demonstrated an equally high incidence of alcoholism and sociopathy as adults. Similar findings were reported by Morrison and Stewart (1971) in their evaluation of parents of 59 hyperactive and 41 normal children. One third of the parents of hyperactive children exhibited a psychiatric or behavioral disorder usually consisting of alcoholism, sociopathy, or hysteria; over 10 percent of the hyperactive children had at least one parent with a history of childhood hyperactivity.

Adoption, sibling, and twin studies have also added further evidence of a genetic transmission of vulnerability to this disorder. Using a systematic psychiatric examination, Morrison and Stewart (1973) and Cantwell (1975*b*) compared the incidence of psychiatric disorder found in the nonbiological parents of adopted hyperactive children to that of the biological parents of nonadopted hyperactive children. (The biological parents of adopted hyperactive children were not available for examination.) These studies found no greater prevalence of a psychiatric disturbance or of childhood hyperactivity among the adoptive parents than existed in the parents of control children. A comparison of the incidence of "minimal brain dysfunction" (MBD) in full- and half-siblings of 17 MBD children found that while 52.6 percent of their full-siblings appeared to demonstrate MBD, only 9.1 percent of their half-siblings were symptomatic (Safer 1973). Comparisons of activity ratings by parents of 93 sets of monozygotic or dizygotic twins suggested a substantial genetic component to activity levels (Willerman 1973). However, this study did not distinguish activity level from the diagnosis of attention deficit as a complete syndrome.

While these studies do not determine the extent of genetic and environmental influences in the transmission and expression of ADD, they do suggest a possible genetic component to the vulnerability for this disorder in some children. The mechanism of inheritance is not clear since father-son transmission and variable penetrance appear likely. Familial studies have not yet clarified what is transmitted: an impaired ability to modulate impulses, an increased level of energy or aggression, or a more specific disruption of attentional or motoric integration. The evidence for substantial genetic contribution to chronic multiple tics of Gilles de la Tourette syndrome, in which motor and attentional disturbances coexist (Kidd, Prusoff, and Cohen 1980), and the suggestion that obsessive-compulsive disorders may have an inherited component further buttress the impression that some biological substrate affects these modulating processes.

Whether or not the diverse components of activity and attention in this disorder are inherited as separate but potentially coexisting factors is unclear. Sexual differences in activity and aggressiveness may contribute to differences in hyperactivity among children with similar attentional diffusion. The suggestion of a genetic factor in this disorder or in its specific components provides impetus for further study of chromosomes, enzymes, and neurotransmitters which may convey this vulnerability.

Biological Factors in ADD. Other lines of evidence suggest a possible biological substrate for ADD with hyperactivity (ADDH). The findings of increased minor physical anomalies among attentionally impaired, hyperactive children may evidence a genetic disturbance or an *in utero* disruption of physical as well as cognitive-integrative integrity. Waldrop and Halverson (1971) found an increased incidence of minor physical anomalies (stigmata) among those nursery school children having higher levels of activity and aggressivity. Rapoport, Quinn, and Lamprecht (1974) documented the presence of multiple minor physical anomalies in 76 severely hyperactive boys. High stigmata scores were associated with teachers' ratings of "hyperactivity" and conduct problems. High stigmata scores were also associated with fathers' history of childhood behavior disorders and with mothers' history of obstetrical difficulties. In addition, plasma dopamine-β-hydroxylase (DBH) showed a significant positive relationship with stigmata scores. These findings suggest the possibility of a genetic disorder that may be mimicked (phenocopied) by a traumatic event in early pregnancy.

The frequency of delayed development of gross and fine motor coordination in children with ADDH provides another possible marker of a biological substrate. However, not all children with attentional deficit have impaired motor coordination, and many children with coordination difficulties are intact cognitively, or exhibit no other psychiatric diagnoses (Rie et al. 1978; Shaffer 1978). "Soft" neurological signs may be developmentally or age-related (Adams, Koesis, and Estes 1974) and are reliably elicited, persistent, but nonspecific; their clinical significance is not clear (Shaywitz 1982). Dysgraphia has been identified in 10 percent, dysdiadochokinesia in 8 percent, and mirror movements in 14 percent, and choreiform movements have been elicited in 11 percent of children without learning or behavioral difficulties (Stine, Saratsioter, and Mosser 1975; Shaffer 1978).

Several investigators have reported that hyperactive children have a higher incidence of nonspecific EEG abnormalities which are not influenced by stimulant medications (Klinkerfuss et al. 1965; Capute, Niedermeyer, and Richardson 1968; Klinkerfuss et al. 1965; Satterfield et al. 1973*a*; Satterfield, Cantwell, and Satterfield 1974). Computer-assisted spectrum analysis of the EEG has suggested some drug effects (Itil and Simeon 1974).

Differences in peripheral autonomic nervous system responses may also suggest a physiological basis for this disorder in some ADD children. Investigators have reported lower levels of spontaneous skin conductance, increased variability and delay in reaction time, and decreased responsivity to an orienting stimulus in ADD. Furthermore, the finding of normal brain morphology using computerized axial tomography in approximately 100 ADD children (Caparulo et al. 1981) suggests that if abnormalities in CNS morphology do exist in ADD, they are not apparent using current techniques. New neuroradiological diagnostic procedures (positron emission tomography, nuclear magnetic resonance) may be useful in demonstrating abnormalities in ADD.

Effect of Stimulants on Catecholamines. Stimulant medications have been widely used in the treatment of ADDH. While amphetamine and methylphenidate have similar effects, amphetamine is approximately twice as potent clinically as methylphenidate. Although stimulants do not improve all aspects of the clinical problem, understanding their pharmacological mechanisms may illuminate some neurochemical components of ADDH. In animal studies, *d*-amphetamine and methylphenidate also produce similar behavioral and CNS activation. Stimulants affect animal learning and activity levels. In high doses they increase stereotyped gnawing behavior in rats, probably a dopamine-related phenomenon.

Stimulant medications have multiple effects on CNS neurotransmitters (Smith and Davis 1977). Amphetamine releases newly synthesized (reserpine-resistant) dopamine and blocks presynaptic reuptake of dopamine and norepinephrine (Clemens and Fuller 1979). Although *d*-amphetamine has more potent effects on norepinephrine release and reuptake than does methylphenidate, they are nearly equipotent in stimulating dopamine release (Ferris, Tong, and Maxwell 1972). Methylphenidate preferentially stimulates release of previously synthesized (reserpine-sensitive) dopamine from vesicular stores (Scheel-Krüger 1971; Davis 1973; Costall and Naylor 1974).

Serotonin modifies and may mediate some of the effects of stimulants. The locomotor hyperactivity induced in rats by intraperitoneal amphetamine was reduced by serotonin injection into the nucleus accumbens, a site rich in dopamine receptors. Lesions of the medial raphe nucleus, which deplete mesolimbic serotonin, enhanced amphetamine-induced hyperactivity (Costall, Hui, and Naylor 1979).

Biochemical Studies of ADD. Given the clinical homogeneity of ADD, the vagueness of the concept of attention, and the variability in activity level among attentionally impaired children, it is not surprising that attempts to define a neurochemistry remain rudimentary. Stimulant effects are not a chemical mirror of the mechanisms of attentional deficit since the medications provide only partial improvement of attentional and behavioral disturbance.

Enzyme Studies of ADD. Dopamine-β-hydroxylase (DBH), the catalytic enzyme which converts dopamine to norepinephrine, is released from the dendritic vesicles into the circulation where it may be assayed. Its wide variability (over 100-fold) in normal populations and its increasing levels during early childhood complicate the determination of normal values (Freedman et al. 1972; Young et al. 1980). Rapoport, Quinn, and Lamprecht (1974) found that while hyperactive children with the highest scores for minor physical anomalies had increased levels of plasma DBH, no direct correlation existed between DBH levels and hyperactivity. The finding of normal DBH levels in a group of children with ADD was verified by subsequent investigation by our group (B.A. Shaywitz et al., in press). Methylphenidate and imipramine treatment appear to increase DBH levels (Rapoport, Quinn, and Lamprecht 1974), but our observations suggest that this is uncertain.

Platelet monoamine oxidase (MAO) is a well-studied enzyme under genetic control. Low levels of platelet MAO may be a source of nonspecific vulnerability to various major psychiatric illnesses (Murphy and Donnelly 1974). MAO, Type A, found in plasma, oxidizes norepinephrine and serotonin, but not dopamine. MAO, Type B, is found in platelets and oxidizes dopamine (Youdim et al. 1972). Platelet MAO activity varies with age and sex; it is greater in girls than boys. MAO levels tend to decrease from infancy throughout childhood, and then increase from late adolescence throughout the adult years (Roth, Young, and Cohen 1976; Robinson and Nies 1980; Young et al. 1980). A similar pattern exists with brain MAO.

In contrast to reduced levels of platelet MAO in chronic schizophrenia (Wyatt and Murphy 1976), normal levels have been found in our studies of autistic children (Cohen, Young, and Roth 1977). In our recent measures of MAO, it is suggested that most children with ADD exhibit normal platelet concentration, although a subgroup with reduced activity may exist.

Cerebrospinal Fluid (CSF) Studies. Determination of amines and metabolite levels in the CSF offers the possibility of obtaining specimens more closely reflective of brain than of peripheral function. The low concentrations of these substances require sensitive assay methods, usually using gas chromatography-mass spectrometry or high performance liquid chromatography (HPLC). Levels of the acid metabolites (HVA and 5-HIAA) can be increased by competitive blocking of their egress through prior administration of probenecid. The levels of these metabolites will increase in approximate proportion to the CSF concentration of probenecid until blockage becomes nearly complete. Subsequent metabolite accumulation may provide an index of dopamine and serotonin turnover rate (Young et al. 1982).

Shetty and Chase (1976) measured CSF homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA), the major metabolites of dopamine and serotonin, respectively, in 24 hyperactive children (19 boys and 4 girls, ages 2–13) without probenecid loading and compared these to six control subjects. Assays were performed by a fluorometric method. Shetty and Chase (1976) found no difference between patients and controls in baseline levels of either acid metabolite. Following 2–14 days of treatment with 0.5 mg/kg *d*-amphetamine in 10 patients, they found a 34 percent reduction of CSF HVA; a slight but inconsistent increase occurred in 5-HIAA. The degree of clinical improvement on medication correlated highly with the reduction of HVA. These changes in HVA with treatment may reflect feedback inhibition of dopaminergic activity and inhibitory serotonergic compensation.

Shaywitz, Cohen, and Bowers (1977) examined CSF levels of HVA and 5-HIAA in six children diagnosed as MBD (boys, ages 5–11; mean =7.5 years) compared to 16 controls who had other neurological difficulties. After probenecid loading (100–150 mg orally), a lumbar puncture was performed. A significant positive correlation between probenecid and HVA levels was found. While the average level of CSF HVA in

MBD children was only slightly below that found in controls, the concentration of HVA (ng/ml) per unit of probenecid (μg/ml) was found to be significantly lower in children with MBD (mean = 9.8 ± 1.5) than in controls (16.5 ± 1.5). CSF 5-HIAA levels did not significantly differ in MBD children and controls.

Urinary Metabolite Measures in ADD. Since urinary samples contain the composite excretions of amines originating predominantly from peripheral rather than brain metabolism, the implications of urinary findings for CNS function are obscure. Although 3-methoxy-4-hydroxyphenylglycol (MHPG), is the primary metabolite of brain norepinephrine, it also reflects peripheral noradrenergic metabolism. Recent estimates suggest that about 60 percent of urinary MHPG is of central origin (Maas et al. 1979). Even though much of urinary MHPG is of peripheral origin, its relative amount may reflect the influence of central noradrenergic activity on peripheral function.

In the initial study of urinary amine metabolites, Wender et al. (1971) measured the 24-hour excretion in nine children (7 to 13 years old) diagnosed as having minimal brain dysfunction (MBD) on the basis of behavior difficulties at home and learning difficulties in school. Their amine excretion was compared to levels from normal age- and sex-matched controls. No differences were found between the groups in the 24-hour excretion of the serotonin metabolite, 5-HIAA, in the DA metabolite, HVA, or in the noradrenergic metabolites, MHPG, vanillylmandelic acid, metanephrine, and normetanephrine. Following a 1-week treatment with *d*-amphetamine, 10–20 mg/day, the MBD group demonstrated an increased excretion of epinephrine and metanephrine but no change in urinary MHPG and HVA levels.

Noradrenergic mechanisms have been investigated further in ADD by Shekim, Dekirmenjian, and Chapel (1979), who compared 15 hyperactive boys to 13 controls, ages 7–12, all with Wechsler Intelligence Scale for Children (WISC–R) IQ scores above 80. Diagnosis of ADD with hyperactivity was established according to *DSM–III* and the Children's Diagnostic Scale of NIMH. Soft neurological signs were quantified using the Physical and Neurological Exam for Soft Signs (PANESS). Two 24-hour urine collections for MHPG were obtained before and 2 weeks after treatment with *d*-amphetamine .5 mg/kg/day. MHPG was analyzed utilizing electron-capture gas-liquid chromatography according to the methods of Maas et al. (1973).

The MBD group excreted lower pretreatment levels of MHPG than did controls (mean ± SD = 1.35 ± .49 micrograms per milligram of creatinine vs. 1.69 ± .33). Following amphetamine treatment, the mean MHPG levels decreased to .95 ± .44. Nine of the 15 MBD children demonstrated improved scores on the Connors Teachers Rating Scales (Factors I and IV) following *d*-amphetamine treatment, while the remaining six showed no significant change. Treatment with *d*-amphetamine decreased urinary MHPG production in the responders (1.40 to .78) while no significant change occurred in the MHPG of nonresponders. In three of the nonresponders, the MHPG actually increased following *d*-amphetamine treatment. Pretreatment levels of urinary MHPG were not predictive of clinical response. However, the presence of soft neurological signs was predictive of improved classroom behavior during amphetamine treatment.

In another study, eight boys with ADDH treated with *d*-amphetamine (.75 mg/kg/day) showed progressive decreases in 24-hour urinary MHPG secretion as measured on the third and eighth days of treatment. Seven of these eight children demonstrated improved classroom behavior on teachers' ratings of hyperactivity; five of these boys showed a significant decrease in urinary MHPG. The one child whose MHPG increased showed no improvement on teachers' behavior rating. Urinary HVA was not altered by amphetamine treatment (Brown et al. 1981).

Serotonin Systems. Disturbance in serotonin systems also has been implicated in ADD. Wender (1969) studied 14 children diagnosed as having MBD and could find no correlation between peripheral serotonin levels and hyperactivity. In three patients, however, diminished serotonin appeared to correlate with excessive hyperactivity. In a subsequent study, Wender et al. (1971) found diminished platelet serotonin levels in approximately 50 percent of children with MBD. Coleman (1971) determined serotonin concentration in whole blood of 25 hyperactive children. A decreased concentration of platelet 5-hydroxyindole was found in 88 percent of this group. Two of the more severely affected patients who subsequently demonstrated increased attention span following milieu therapy showed an increase in peripheral 5-HIAA, suggesting an association between diminished serotonin and hyperactivity. Rapoport, Quinn, and Lamprecht (1974) found normal blood serotonin levels in hyperactive children. While both methylphenidate and imipramine improved behavior, imipramine alone lowered blood serotonin levels. Other studies in children who were both hyperactive and retarded showed that they had lower blood serotonin levels than controls. Serotonin appeared to increase as behavior improved following nondrug treatment regimens (Greenberg and Coleman 1976).

Recent methodological advances in the preparation of platelets and the assay of serotonin may clarify further the role of indoleamines in this disorder. Previous techniques of platelet centrifugation to obtain platelet-rich plasma suffered from variability in the type and percentage of platelets recovered. Improved ability to lyse platelets, and thereby free all serotonin, and the development of a simplified assay of plasma serotonin using HPLC provides renewed impetus for further examination of serotonin levels in ADD (Anderson and Young 1981; Young et al., in press).

Recent analytical techniques enable concurrent assays of several neurochemicals within and across neurotransmitter systems. Simultaneous indices of synthesis, release, catabolism, and receptor response along the pathway of a functional neurotransmitter system can be obtained. Such a map or equation is best generated in response to a controlled pharmacological stress or stimulus which has considerable neurochemical specificity of action. By stimulating or inhibiting the system at a specific point and monitoring the response or impact at other moments, one can generate a map of neuronal sensitivity. Concurrent or sequential measures of crucial loci along a functional system allow individual determinations to be placed within the context of the tone or responsiveness of their neurotransmitter system. This strategy attempts to identify alterations in the modulation and sensitivity of a neurotransmitter system rather than a high or low concentration.

An index of presynaptic functioning can be obtained by determination of synthesizing enzymes (e.g., tyrosine hydroxylase, dopamine-β-hydroxylase), by dietary loading (tryptophan enhancement of serotonin), or by precursor administration (L-dopa stimulation of dopamine). Depletion of the precursor (e.g., reserpine release) or inhibition of catecholamine synthesis through destruction of selected neuronal systems (e.g., inhibition via 6-OHDA administration, electrolytic lesions, on enzyme blockade with FLA-63, or disulfiram) can alter presynaptic synthesis. Turnover of presynaptic neurotransmitters can be estimated by the accumulation of the acid metabolites following probenecid blockade from the CSF. Timed urinary collections of MHPG provide an estimate of CNS noradrenergic release (Maas et al. 1979). Postsynaptic receptor sensitivity may be estimated by measures of response to secondary messengers, such as amine-specific cyclic 3′,5′-adenosine monophosphate (AMP) to receptor stimulation, or by determination of physiological response, such as platelet aggregation (Daly 1976). Pharmacological probes and neuroendocrine strategies may provide another window into CNS amine functioning.

Pharmacologic Probes and Pharmacokinetics

Approximately 200,000 to 500,000 children in the United States receive stimulant medication for attentional and behavioral control. The recent development of a sensitive assay for methylphenidate enables the quantification of blood levels and the determination of the pharmacokinetics of methylphenidate in children. Blood level determination may have therapeutic utility in identifying children who absorb methylphenidate poorly or excrete it rapidly and thereby fail to achieve adequate levels. Blood levels of methylphenidate, when coupled with sequential plasma measures of catecholamines and hormones, may provide a pharmacological probe of the responsiveness of these neurochemical systems. Repeated measures of methylphenidate absorption and neurotransmitter or peptide response during the course of drug treatment may identify shifts in drug absorption and metabolism which affect its bioavailability. An alteration of subsequent neurochemical response during the course of methylphenidate treatment may indicate a drug-induced change in amine synthesis, release, or receptor sensitivity.

In recent studies in our laboratory, 12 boys (age 6.5 to 15, mean ± SD = 11.3 ± 2.8 years) who met *DSM-III* criteria for ADD received oral methylphenidate, .3 mg/kg ± .05 mg/kg. Blood samples were drawn every half hour for 4 hours, then less frequently until 8 hours after medication. The peak level of methylphenidate was reached at a mean time of 2½ hours (± 20 minutes) following oral administration. Considerable individual variance was evident since peak times for individuals ranged from 1 to 4 hours. The mean (±SD) of the peak blood levels achieved was 8.3 ± 3.0 ng/ml. A large variability of peak levels (5.4–14.8 ng/ml) existed across individuals receiving similar methylphenidate doses. There was a tendency for early peaks (those occurring at or before 1.5 hours after administration) to be associated with high peak levels, suggesting more rapid absorption. The excretion half-life (t½) of methylphenidate was 2.5 ± .5 hours. Repeated blood level curves obtained following the same dose of methylphenidate in children treated for 6 weeks showed a high replicability when compared to blood levels obtained after their first dose.

Substantial blood levels of methylphenidate persisted at 4, 5, and 6 hours following administration; measurable levels were common at 8 hours. Thus, the blood level remained significant even after the optimal clinical effect had passed. This lack of a simple correlation between blood level and clinical effect probably reflects the mechanism of action of methylphenidate. It rapidly facilitates the release of stored catecholamines and has relatively less direct stimulating effect on postsynaptic receptors. Thus, high methylphenidate levels persisting after the initial release of catecholamines might be expected to have diminished effect. These results are compatible with a pharmacological study of methylphenidate (Hungund et al. 1978) on four children with ADD.

In a related study of methylphenidate blood levels during chronic treatment, single methylphenidate measures were obtained at 1 and 2 hours following the child's regular outpatient dose. Children whose behavior ratings improved during treatment had significantly higher blood levels of methylphenidate than those who did not show behavioral improvement (S.E. Shaywitz et al., in press).

A somewhat different pharmacokinetic profile was noted in studies of *d*-amphetamine performed at the National Institute of Mental Health using a reliable, sensitive radioimmunoassay (Cheng et al. 1973; Ebert, van Kammen, and Murphy 1976). The pharmacokinetics of *d*-amphetamine was evaluated in 16 ADD boys following a single dose of about .5 mg/kg. Peak *d*-amphetamine concentrations (mean ± SD = 65.9 ± 4.6 ng/ml) occurred 4 hours after oral administration. The elimination half-life (t½) was about 6.8 ± 0.5 hours. Behavioral improvement, rated on the Conners abbreviated 10-item scale, was significant from 1 to 4 hours after medication. The decrease in restless motor activity usually occurred before the peak level of amphetamine was reached. The greatest variability in blood level occurred during the absorption phase. Since the maximal behavioral improvement occurred during the absorption phase, no simple correlation between absolute blood level and behavioral response emerged. Retest of six children with the same *d*-amphetamine dose showed no significant difference in absorption or elimination 1 week later (Brown et al. 1979*a*).

Neuroendocrine Response to Stimulant Medications

Neuroendocrine provocative tests provide a means of assessing the responsivity of the hypothalamic-pituitary axis. Hormonal responsivity to a pharmacological stimulus with well-defined neurotransmitter effects may provide an index of receptor sensitivity and may reflect the integrity of processes affecting peptide synthesis, storage, or release. This strategy has been used in a preliminary manner to characterize ADD.

Neurotransmitter Regulation of Prolactin and Growth Hormone. Increasing evidence illuminates the prominent role of neurotransmitters in the regulation of pituitary hormone release (Anton-Tay and Wurtman 1971; Sachar 1976; Martin 1976; Rose and Ganong 1976). Pharmacological agents with specific well-defined effects on neurotransmitter systems have been used to dissect these mechanisms (MacLeod and Lehmeyer 1972; Donoso, Bishop, and McCann 1973).

Prolactin and growth hormone are regulated by catecholamines and indoleamines. Prolactin secretion is inhibited by dopamine stimulation (McCann et al. 1972; Hyppa and Wurtman 1973; Sachar and Clemens 1974). Both synthesis and secretion of prolactin are inhibited by norepinephrine (MacLeod and Lehmeyer 1972), although large doses may have the opposite effect. Serotonin appears to stimulate prolactin secretion when given intraventricularly or systemically. Thyroid-releasing factor (TRF) also stimulates release of prolactin (PRL). This effect is decreased by thyroxine and L-dopa and enhanced by estrogens. PRL may be under dual regulation, with prolactin inhibitory factor (PIF) being stimulated by dopamine and prolactin-releasing factor (PRF) being inhibited by serotonin.

Human growth hormone (HGH) is stimulated by dopamine and norepinephrine (Martin 1973; Eddy et al. 1974; Lovinger et al. 1975; Martin et al. 1975). α-Adrenergic stimulation, as with clonidine, increases HGH (Leckman et al. 1980). Phentolamine, an α-adrenergic antagonist, suppresses the L-dopa-stimulated rise in HGH (Kansel et al. 1972), while propranool, a β-adrenergic blocker, enhances the rise in HGH which follows a variety of stressors (Frohman and Stachura 1975). Dopaminergic and serotonergic drugs promote HGH release; drugs which block or inhibit these neurotransmitters usually decrease growth hormone (Sachar 1975).

Drugs which diminish synaptically available dopamine by depleting dopamine stores—for example, reserpine (Ratner, Talwalker, and Meites 1976)—or which block dopamine postsynaptic receptors—for example, haloperidol (Dickerman et al. 1974) or chlorpromazine (Kleinberg, Noel, and Frantz 1971)—elevate prolactin or diminish growth hormone (Clemens, Smalstig, and Sawyer 1974). Drugs which stimulate dopamine receptors—for example, apomorphine (Brown and Reichlins 1972; Martin et al. 1974; Lal et al. 1975)—or increase synaptically available dopamine—for example, L-dopa (Donoso, Banzan, and Barcaglioni 1974)—decrease prolactin and stimulate growth hormone (Kansel et al. 1972; Lal et al. 1975).

Hormonal Effects of Stimulant Medication. The effect of stimulant medication on pituitary hormone response has been studied in animals and in psychiatric illnesses of man. Marantz et al. (1976) noted growth hormone stimulation following i.v. *d*- and *l*-amphetamine administration in monkeys. Brown and Williams (1976) observed a marked elevation of HGH in schizophrenic patients who were not receiving neuroleptics following i.v. administration of .5 mg/kg methylphenidate. Growth hormone response to stimulation with L-dopa has been found to be relatively attenuated in depressed patients (Sachar 1976). Langer et al. (1976) found that patients with endogenous depressions demonstrated a smaller HGH release following amphetamine administration than did patients with reactive depression or schizophrenia. Brown (1977) found HGH release in 17 normal males following methylphenidate administration (10 or 20 mg orally) correlated highly with their subjectively experienced euphoria. Janowsky, Parker, and Leichner (1976) observed a significant elevation of HGH in schizophrenic patients, many of whom were receiving neuroleptics, following i.v. administration of .5 mg/kg methylphenidate. Janowsky and Davis (1976) found a similar significant increase in plasma HGH following i.v. methylphenidate in a mixed group of psychiatric patients. Brown et al. (1978) gave oral methylphenidate (10 or 20 mg) and *d*-amphetamine (10 or 20 mg) to 50 normal male volunteers and found that their HGH was stimulated by both drugs. At the higher amphetamine dose, HGH levels correlated with amphetamine blood levels and with subjectively reported euphoria. Methylphenidate decreased the elevated prolactin levels in schizophrenic patients receiving neuroleptics. Cortisol was elevated following amphetamine alone and also correlated with subjective arousal. PRL is inhibited by dopamine and increased by dopamine-blocking agents. Amphetamine (5 mg/kg), but not methylphenidate (10 mg/kg), blocks the increase of serum prolactin in reserpine pretreated male rats (Clemens and Fuller 1979). Amphetamine lowered, while methylphenidate increased, brain 3,4-dihydroxyphenylacetic acid (DOPAC) in control rats.

Neuroendocrine Studies in ADD. Few neuroendocrine studies have been performed in children with ADD. Aarskog, Fevang, and Klove (1977) gave single doses of either L-dopa (sinemet), approximately 10 mg/kg, methylphenidate, 20 mg, or *d*-amphetamine, 15 mg, to 20 hyperactive children and measured HGH response at 30-minute intervals for 3 hours. They noted a similar pattern of HGH release and peak (at 60 to 90 minutes) in all treatment conditions. After 6- to 8-month treatment with methylphenidate, seven children were retested with L-dopa and *d*-amphetamine provocation 24 hours after their last methylphenidate dose. Their baseline HGH levels after chronic treatment with methylphenidate were elevated and response to *d*-amphetamine was diminished at 30 to 60 minutes.

Using methylphenidate as a pharmacological probe in ADD boys to examine the responsivity of the hormone and amine systems, we obtained sequential half-hourly measures of HGH, PRL, norepinephrine, epinephrine, and dopamine from plasma and correlated these with the concurrent levels of methylphenidate. HGH concentration increased and PRL decreased concurrent with the peak level of methylphenidate; plasma catecholamines tended to decline following administration of this stimulant (S.E. Shaywitz et al., in press).

Clonidine in ADD. Clonidine, an α-adrenergic agonist, given as a single oral dose with subsequent plasma measures of HGH, catecholamines, and their metabolites, may help define the responsivity of noradrenergic and dopaminergic systems in ADD. In low doses, clonidine acts preferentially on the presynaptic norepinephrine receptor to diminish endogenous release of norepineprhine (Stark and Montel 1973). The effect of clonidine on plasma norepinephrine and MHPG in ADD children compared to age-matched controls may be indicative of their noradrenergic tone or sensitivity (Leckman et al. 1980). Responsivity may be altered by treatment or withdrawal from stimulant medication. In our preliminary observations on boys before and during treatment with methylphenidate, the degree of stimulation of HGH release following administration of a controlled dose of clonidine may be an index of the sensitivity of this neuroendocrine axis. This could further clarify the mechanism of growth suppression in children chronically treated with high-dose stimulant medication (Cohen et al. 1979; Gil-Ad, Topper, and Laron 1979). The responsivity of the neuroendocrine system to acute clonidine, however, may not parallel the response of central brain noradrenergic receptors.

Clonidine is also a potential therapeutic agent for some children with ADDH. The need for therapeutic alternatives to stimulant medication is evident from the side effects of stimulants (irritability, growth impairment), contraindications (e.g., tics), and from the limited benefit often seen from treatment with medication alone (lack of improvement in academic achievement). A double-blind, crossover study of clonidine and placebo in 37 children with ADD suggested clinical improvement in ratings of hyperactivity, attention, learning, and impulsive behavior (Lechin et al., in press). We have completed an open therapeutic pilot study of four children (9–14 years) with ADDH given clonidine 3–4 μg/kg/day for 2–5 months. Parent and teacher ratings suggested improvement in the Hyperactivity Index from the Conners Scale. Parents noted that their children were calmer, more compliant, and had increased frustration tolerance. Distractibility often continued, but subjects were more able to return to and complete a task (R.D. Hunt, D.J. Cohen, and S.E. Shaywitz, personal communication, 1982).

Summary and Speculations

Attention deficit disorders (ADD) describe several clusters of children who share symptoms of short attention, impulsivity, and motoric hyperactivity. The role of attention and cognition as a core influence in personality development makes the study of ADD germane to understanding many psychiatric syndromes. Human and animal studies suggest the importance of catecholamines, indoleamines, acetylcholines, and hormones in the interlocking processes which constitute attention, activity, arousal, and memory. Since attentional disorders may follow disruption of perceptual or integrative functions, there may not be a unique neurochemistry underlying the complex syndrome of ADD. The pattern of neurochemical disturbance may reflect the severity as well as the source of disturbance within a predominant clinical subtype. Among children whose symptoms fall under the broad umbrella of ADD, some have primary disturbance in activity level; others may be primarily explosive, impulsive, or episodically aggressive; still others are primarily inattentive and distractible but demonstrate minimal disturbance in activity, aggression, or mood; and another subgroup exhibits predominant fluctuation in mood. The phenotypic expression of the varied genotypes or substrates may be difficult to dissect in the classroom or to evaluate in the playroom but may reflect varying neurochemical equilibriums within the brain.

Static or state measures of these and other neurotransmitters may not reflect their functional significance. The use of discrete pharmacological probes with well-established neurochemical mechanisms of actions, correlated with acute behavioral, attentional, and chemical response, may define further the relationship between neurochemical substrates and attentional processes.

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Genetic Strategies for the Analysis of Childhood Behavioral Traits

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Abstract

Genetic strategies appropriate for the analysis of childhood behavioral traits are reviewed. The problem of etiologic heterogeneity is discussed, and suggestions for minimizing its effect are offered. Two traits, stuttering and Tourette syndrome, are given as examples to illustrate methodologies useful for the genetic analysis of childhood disorders. In both examples, it is shown that the disorder clusters in families, that it is vertically transmitted, and that the transmission is sex-modified. Several genetic models can explain the pattern of transmission, although cultural hypotheses also should be considered. Hence, additional analyses need to be attempted to help clarify the modes of transmission and the factors involved.

The genetic element of a disease is obvious if an enzyme or structural protein is altered or absent. Certain other biochemical aberrations are presumptive evidence of genetic defects even in the absence of family data. However, for most childhood behavioral disorders, biochemical studies have not yet provided evidence for any genetic defect. Four other types of evidence can suggest that genetic factors are responsible for a disease of unknown etiology: (1) a higher concordance among monozygotic (MZ) twins than among dizygotic (DZ) twins; (2) significant aggregation of the illness within families; (3) genetic linkage of the illness with an identifiable allele at a marker locus; (4) a higher incidence of the trait among biological offspring of affected individuals that among biological offspring of unaffected individuals, even when those children have been raised in adoptive homes.

Twin studies and studies of biological families may yield data suggesting genetic involvement, but such data are incapable of proving the existence of genetic factors for any traits that might have a major environmental component in their etiology. Genes and familial environment are confounded in determining similarities among relatives and cannot be separately quantified. For this reason geneticists today stress the distinction between familial and nonfamilial environmental factors as well as the possibility of confounding familial environmental similarity with genetic similarity among relatives (Cavalli-Sforza and Feldman 1973; Rao, Morton, and Yee 1976; Kidd and Matthysse 1978; Rice, Cloninger, and Reich 1978; Cloninger, Rice, and Reich 1979). The familial environmental factors that come most readily to mind include those that tend to be shared by all members of a family, such as religion, language, and diet. Actually, most environmental factors show some familial aggregation, but the degree of their concentration in families varies considerably. Among the environmental factors showing a familial concentration, some, especially the cultural ones, can actually be transmitted, like genes, from parent to child. In practice, it may be very difficult to distinguish cultural from genetic transmission.

One of the strongest forms of evidence for a genetic factor is the

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demonstration of genetic linkage. Genetic linkage is detectable, at least in theory, if a known genetic marker locus is sufficiently close to a locus segregating for alleles affecting the trait that nonrandom segregation of alleles at the two loci results in an association of phenotypes within a family. Thus, if it is possible to demonstrate genetic linkage between a hypothesized locus for a disorder and a well-known marker locus, that demonstration provides convincing evidence that there is a major gene contributing to the disorder since it is highly unlikely that any other explanation could mimic linkage with a marker locus.

Some problems in detecting linkage in human data include fairly small family sizes, inability to control matings, and the small prior probability that two loci are linked. In addition, linkage studies are often not efficient since only a small proportion of families studied will actually show segregation for any particular marker locus. Other problems with linkage studies have to do with the disorder in question. The presence of reduced penetrance and a variable age of onset will reduce the power of the statistical methods that have been developed to test for linkage. Most of these methods assume high penetrance for the trait being studied. The program LIPED version 3 developed by Ott (1976) allows for incomplete penetrance and, in addition, has been modified to allow for sex- and age-dependent penetrance values (Hodge et al. 1979).

Adoption or separation studies also can give evidence for a genetic factor. If a trait is genetic, then children should more closely resemble their biological relatives than they do their adoptive relatives. Separation studies also provide the ability to see to what extent environment influences the trait in question. If the children resemble their adoptive parents and siblings to any extent, then that resemblance is, at least in theory, due to environmental similarities. It may then be possible to partial out some of the environmental and genetic influences of the trait being studied.

There are some difficulties with adoption studies. Very often the adoptive children are put in homes that closely resemble the homes of the biological parents. Hence, when comparisons are made between child and biologic parent, the similarity may result from selective placement and not genetic contribution (Munsinger 1975). It may be that for serious psychiatric problems this may be less of a problem than for traits like IQ. However, it is a problem that needs to be noted. Another problem with separation studies is that it is often difficult to get adequate data on the biologic parents. Since these studies tend to be retrospective, information necessary for diagnoses needs to be derived from records obtained when the mother was pregnant. Often the information is not adequate. Also, to do a good genetic analysis, information from both parents is necessary. Unfortunately, much of the time information on the biologic father is missing completely.

Still another difficulty with adoption studies is that the information obtained will not allow any statements about possible mode of transmission. Unless information is available about other biologic siblings of the adoptive children, nothing can be said about how the trait might be transmitted. Hence, adoption studies as well as genetic linkage studies can demonstrate that genetic factors must be important, but such studies are difficult to conduct and are not commonly done. Even when done, they can still give ambiguous results.

In the absence of a well-understood etiology, demonstration of the presence of genetic factors does not usually resolve questions about the nature of the genes involved and how they interact with environmental factors. For example, the adoption studies of adult schizophrenia (Heston 1966; Rosenthal et al. 1971; Kety et al. 1975) have provided strong evidence for a genetic component to schizophrenia, but many questions still remain. Is a particular gene necessary for the disease to develop? Will a certain genotype always lead to illness? Are there ameliorating environments that prevent illness in persons otherwise susceptible? Answers to questions such as these usually require data of many different types. Adoption studies and comparisons of MZ and DZ concordances provide little, if any, information on these questions. Family segregation patterns (how many and which specific relatives are affected) with or without genetic linkage do provide relevant information and may provide partial answers. However, the full scope of gene-environment interactions can only be understood after the full disease process is understood. Until such a time, family data—pedigrees—and data on genetic linkage can be the bases for an initial understanding.

Possible Complications

Etiologic Heterogeneity. In the design of both psychological and biological studies, it is essential to consider that the disorder being studied may be heterogeneous. Heterogeneity can be present at several different levels. When a syndrome subdivides into distinct classes by onset, course, or response to treatment, a corresponding heterogeneity in etiology is a possibility that must be considered. For example, it is likely that infantile autism is a behavioral syndrome with multiple etiologies (Rutter 1974). It is known that the syndrome can develop in association with conditions as pathologically diverse as congenital rubella (Chess, Korn, and Fernandez 1971) and infantile spasms (Taft and Cohen 1971). These environmental agents may be causal in these cases, but infantile autism can also develop in the absence of any environmental agents such as these. Hence, the search for possible genetic factors for autism must take into account the likely etiologic heterogeneity. For example, recurrence risks in these families of autistic children should be calculated separately according to environmental factors present and compared to risks in families with no known causes for the disorder.

An apparently homogeneous syndrome may also be heterogeneous, with quite different etiologies producing nearly indistinguishable symptoms. For example, the mucopolysaccharide storage diseases encompass defects of seven different enzymes. Initially, all affected children were considered to have "gargoylism." Now the symptoms for most of the defects are recognized to be different, largely as a result of biochemical/genetic differences having been demonstrated. However, two different enzyme deficiencies give rise to clinical disorders that are still indistinguishable except by enzyme assays (Kolodny 1976). Often, the multiple causes of a "single disease" become easily identifiable as new phenotypic levels are defined: What is apparently homogeneous at the level of gross symptomatology becomes obviously heterogeneous as physiological and/or biochemical aberrations are used to redefine the phenotype. There are many other examples of genetic heterogeneity, the same phenotype being caused by defects at different gene loci, e.g., hemophilia, congenital deafness, and anemia (McKusick 1975).

Various types of heterogeneity may be confounded. For example, several different genetic types may exist, and each may have its own separate array of environmental precipitants. Diabetes may be such a disorder, with different modes of inheritance for susceptibilities to juvenile-onset diabetes, to the maturity-onset type of diabetes of the young, and to maturity-onset diabetes. Different environmental agents are thought to be involved for each type (Ganda and Soelder 1977), and genetic heterogeneity may also be present within each type. The anemias are another example of multiple etiologies. There are several different genetic types. Some, such as β-thalassemia and hereditary spherocytosis, have pathologic processes largely unaffected by environmental variation. Others, such as favism, are quite susceptible to environmental variation. There are also nongenetic anemias caused by environmental factors, such as iron deficiency.

Minimizing Heterogeneity. Separating out different genetic types solely on the basis of the inheritance pattern is possible for some disorders such as retinitis pigmentosa (Spence, Elston, and Cedarbaum 1974). In this case, most large pedigrees can be placed reasonably well into one of three separate classes: autosomal recessive, autosomal dominant, and X-linked. However, some pedigrees are compatible with both autosomal dominant and X-linked inheritance (Gladstien and Spence 1979). For many disorders there is no obvious heterogeneity among the patterns in different families. For the psychiatric disorders and many other disorders with a reasonably large nongenetic component, no exact Mendelian frequency is expected; some families might show apparent recessive inheritance, while others might show apparent dominant inheritance, simply as a function of chance. To select out pedigrees that appear to represent a particular mode of inheritance, autosomal dominant, for example, is likely to lead to false conclusions. Even in the absence of incomplete penetrance, a mixture of rare recessive and rare dominant pedigrees will be difficult to untangle by pattern alone if the family size is small. Some other techniques for resolving heterogeneity are needed.

Diagnostic Precision. Genetic studies of childhood behavioral disorders—whether twin, family, linkage, or adoption studies—have been hampered by the imprecision and variability of diagnostic criteria. In fact, much variation in results among different studies might be explained by the differences in diagnostic methods. There are several sources of unreliability in diagnosis; we shall consider two.

The first is the method of collecting information necessary for making diagnostic distinctions; here childhood disorders present special problems. In genetic studies, it is desirable to obtain comparable information from all family members regardless of age. This means interviewing adults about their behavior some 20 to 40 years ago. Such retrospective elicitation is necessary because of the transitory nature of symptoms in many childhood behavioral disorders. Often the disorder is outgrown completely; in other cases the symptomatology changes over time. It is difficult to determine if an adult being studied actually had the appropriate symptoms during childhood, but accurate diagnoses are a necessity in genetic studies. Clearly, work needs to be done in this area. A second source of unreliability in diagnosis is in the rules for using the data to classify patients. The systematically collected information on symptoms needs to be used in a precisely defined way to assign valid diagnoses. The problem of validity is one that can be finally resolved only with a complete understanding of the etiology of the disorder, but must still be considered in early research on the disorder.

New diagnostic methodologies that take into account these sources of variation and improve reliability considerably, such as *DSM-III* (American Psychiatric Association 1980), are now being applied to genetic studies. Improved definitions of diagnostic categories and the greater accuracy with which patients can be assigned valid diagnoses will undoubtedly improve future genetic studies. But much work remains to be done. Followup studies are needed to determine whether any relationships exist between childhood and adult behavioral disorders. For example, is the depression seen in children an early manifestation of depression in adults (Orvaschel, Weissman, and Kidd 1980)? Diagnostic criteria should then become available to facilitate more accurate diagnoses. When the use of these diagnostic criteria becomes widespread, the resulting diagnostic uniformity will allow meaningful comparisons between studies.

Sample Definition. After diagnostic criteria have been used to define the phenotype as rigorously as possible, there are additional ways to minimize possible heterogeneity within the data set before any genetic analysis. These are (1) controlling in the sample for possibly relevant nongenetic variables and (2) collecting data from a population as genetically homogeneous as possible. Genetic homogeneity is more likely in a sample from the same ethnic group than in a completely random sample; it is even more likely to exist in an inbred isolate; genetic homogeneity is more likely to be found in a single pedigree. Even in situations that are relatively homogeneous, genotypic heterogeneity may exist among affected, i.e., some are heterozygous and some are homozygous. The frequency of homozygosity may be increased by special ascertainment criteria for families. Matthysse and Kidd (1976) have shown that ascertainment through two affected children changes the expected genotype distribution of the family markedly because the probability of affected individuals being homozygous is increased considerably.

Selecting for additional affected individuals among remote relatives in multigenerational data should enhance etiologic homogeneity and greatly simplify interpretation of biochemical data. However, if those same pedigrees are to be used for a statistical analysis to estimate genetic parameters, the bias introduced by the high-density ascertainment must be estimated and removed. Morton and Kidd (1979) have developed one method for removing the bias from a likelihood procedure for parameter estimation. Their method is impractical for general use because it requires extensive computer simulation, but their results do show the necessity of considering the high-density ascertainment bias.

If homogeneity is achieved by collecting data only from a population with a restricted gene pool (e.g., an isolate or a single pedigree), the results obtained may not extrapolate to the same phenotype in other populations. That should not be a deterrent for special ascertainment strategies, however. If it is possible to identify a specific etiology for a homogeneous group selected with a unique ascertainment technique, it may be possible to establish clinical differences which could then be used to ascertain other groups for additional study.

Another strategy for enhancing possible homogeneity has been suggested by Buchsbaum and Rieder (1979). If a biochemical abnormality has been suggested to be associated with a particular trait, then selecting subjects on the basis of that biochemical phenotype rather than a psychiatric phenotype might enhance homogeneity. After that sample has been selected, psychiatric evaluation may then be done to see if a higher than expected number of these subjects have a psychiatric disorder. As the authors point out, this allows the investigator to determine if a variety of symptomatologies (i.e., a spectrum) is associated with the biochemical abnormality. In childhood disorders the investigator could determine whether the biochemical abnormality remains observable into adult years and what, if any, symptoms are associated then.

Genetic Analyses

Methods. Once homogeneity has been obtained to the best of our ability and the data have been collected, the analysis of the data can begin. The best of the current approaches to genetic analyses of childhood psychiatric disorders and other complex traits is based upon testing of specific genetic hypotheses and attempting to discriminate among the many different genetic models proposed over the past few years (cf. Kidd and Pauls, in press). It is to be hoped that some reasonable set of parameter values for one single model will provide an adequate fit to the observed data while no parameter values for other models will allow acceptable fits. The acceptable model can then be taken, with reasonable confidence, as the true explanation for the genetics of the trait.

There are, however, difficulties with this approach. For example, a familial aggregation that does not appear to follow standard Mendelian inheritance patterns is common for psychiatric disorders (Rosenthal 1970), other behavioral disorders such as stuttering (Kidd and Records 1979), and a variety of birth defects, such as cleft lip and cleft palate (Chung, Ching, and Morton 1974). The simplest explanations of these inheritance patterns incorporate the notion that not all individuals who have a genetic susceptibility actually manifest the disease, i.e., there is incomplete penetrance of the susceptible genotype(s). When twin studies demonstrate that MZ concordance is less than 100 percent, incomplete penetrance can be accepted as a demonstrated phenomenon. Several approaches to genetic analysis of these disorders have been based on incomplete penetrance (Crittenden 1961; Falconer 1965; Morton, Yee, and Lew 1971; Elston and Campbell 1971; Elston and Yelverton 1975; Kidd and Cavalli-Sforza 1973; Morton and MacLean 1974). These models differ in whether the genetic basis is a single major locus or is polygenic (many independent loci, each of small effect), but in every model the susceptible genotypes do not always result in illness. Moreover, most models consider the possibility of phenocopies—individuals in whom the disorder is produced by purely environmental factors in the absence of the susceptible genotypes. These models give rise to different levels of heterogeneity —the same disorder is produced by either a genetic aberration (interactively with the environment) or by purely environmental factors such that patients represent all possible susceptibility genotypes. The incomplete penetrance also results in all genotypes being represented among the unaffected.

Hence, for both theoretical and pragmatic reasons, the model fitting approach has been less than satisfactory. From a statistical perspective the greatest difficulty in the genetic models is the large number of inherent assumptions and simplifications (Kidd 1981). Because of these, the possibility exists that a statistical test may often be testing the validity of the assumptions for a particular trait rather than the applicability of a model's basic genetic mechanism to that trait. From a purely pragmatic perspective, it is now clear that conclusions on a specific mode of inheritance are difficult to reach. Many analyses of real (as opposed to simulated) data have been unable to discriminate between quite different genetic models. Simulation studies have shown that most available types of data on complex disorders do not allow clear discrimination among different genetic hypotheses—most reasonable models are able to explain data on presence/absence of the disorder approximately equally well. Discrimination has so far been reasonably successful only when genetic linkage data or data on obviously related biochemical traits are also incorporated in the analysis (e.g., Kravitz et al. 1979).

To counter this pessimistic conclusion, there are steps that can be taken to improve the outlook for understanding complex disorders such as childhood behavioral traits. One of the most important steps is to choose models that are appropriate to the known biology of the disorder. For example, if sex effects are known to exist, then sex-specific parameters should be included in the analysis. As obvious as this seems, it has not always been done in the past, in part because of limitations in computer methodology. Those limitations no longer exist. Another important step is the preliminary estimation of some parameters using data not included in the genetic analyses. This approach improves the accuracy of estimation for the genetic parameters since, as more parameters are included to make the genetic models more realistic, the precision of simultaneous estimates will be lessened. Of course, some parameters cannot be estimated separately from the genetic model, but others can be. For example, age-of-onset distributions can be estimated using data on unrelated individuals (Heimbuch, Matthysse, and Kidd 1980). Using a "known" distribution as a first approximation in a pedigree analysis should allow a clearer estimation of the remaining parameters and a greater ability to discriminate among alternative hypotheses.

If we momentarily forego the ultimate goal of elucidating the precise roles and interrelationships of all factors relevant to a disorder, and instead consider only more immediate goals, the prospects seem brighter. No one expects a complete understanding of etiology to emerge from one study alone; each study serves to provide insight into the design of further experiments aimed at elucidating etiology. If one merely identifies one significant factor or eliminates one possible hypothesis, the study can be judged successful. In this context, even though our ultimate goal is an understanding of the etiology of the trait, it seems appropriate at the moment to take a "backward" step from precise genetic models and relax the rigor of hypothesis testing. Instead, let us approach family data in the spirit of exploratory data analysis—use of statistics to expose the data to "visual" examination.

Many existing analytic techniques might be considered in the context of exploration rather than testing of specific genetic models. One is Slater's (1966) examination of the distribution of uniparental and biparental occurrences of secondary cases in the ancestry of probands. He suggested that biparental occurrences would represent approximately one third of the cases for polygenic inheritance but be exceedingly uncommon for single-locus inheritance. Little has been done with this measure, but it might be worth more exploration as a quick and simple part of an initial exploratory analysis of a set of data. Another method is the use by Reich et al. (1979) of correlation coefficients and complex segregation analysis to determine whether apparent subtypes of a disorder represent etiologic heterogeneity, part of a genetic continuum, or random variation in the phenotype. Another approach is the use of a logistic analysis (Cox 1970) for study of multiway contingency tables.

The logistic model is related to the log linear model but is considered more appropriate for qualitative data like diagnostic categories (well or affected) among relatives. The model can be used to test whether chance alone can explain the differences in frequencies of affected relatives observed among the subsets defined by classifications used. The objective is the elucidation of patterns of risk among relatives. The method has proved useful for preliminary analysis of family data on human behavioral traits. It has been applied to affective disorders (Smeraldi et al. 1979), stuttering (Kidd and Records 1979; Kidd, Heimbuch, and Records 1980), and Tourette syndrome (Kidd, Prusoff, and Cohen 1980).

Examples of Genetic Analyses. The analyses of data on *stuttering* illustrate many aspects of our approach to the genetics of childhood disorders and its value. The data discussed here were collected in a 5-year study of 600 stutterers and their relatives. The analyses done so far are restricted to the data from probands of European descent. The details of ascertainment and data collection have been presented elsewhere (Kidd and Records 1979). The study accepted only probands with a clinical diagnosis of stuttering and no evidence of any other neurologic problem such as epilepsy and cerebral palsy. Data were collected by interview and self-report questionnaire on presence of stuttering at any time in each first-degree relative.

Several preliminary analyses were done before more complete analysis. Kidd, Kidd, and Records (1978) examined the possible causes for the excess of males among individuals who stutter. The possible factors examined included ascertainment bias, incomplete reporting, social role differences, X-linked inheritance, and a combination of environmental and genetic elements. Only the gene-environment interaction hypothesis was consistent with the data. The sex difference was shown to be real and to be related to transmission of the trait. It was concluded that the sex difference observed should be included in any subsequent analysis aimed at understanding etiology of this trait.

The data were also examined to determine whether some biases in the modes of ascertainment had yielded distinct subsets of the data with sufficient differences that their existence might affect subsequent analyses. Three major sources of data were defined: (1) child probands were obtained primarily through speech pathologists in schools and private clinics; (2) most adult probands were obtained through enrollment in an intensive therapy program; (3) other adult probands were obtained through clinics and the Councils of Adult Stutterers in several large cities. A comparison of the familial incidences of stuttering for each of these three groups, with incidences calculated separately according to sex of relative, sex of proband, and relationship, showed the families of the children to be significantly different from those of the two adult groups. There was no difference between the adult sample from intensive therapy clinics and the other adult sample. However, the families of child stutterers were different from the families of the adult stutterers. Simple tabulation of the frequencies of affected relatives showed that for child probands, parents more frequently had a history of stuttering than they had for adult probands. This is contrary to an intuitive expectation that, because most children who stutter recover before adulthood, childhood stuttering is usually a milder, less severe form than adult stuttering.

Two possible biases could account for the elevated (according to that intuitive expectation) frequency of stuttering among parents of child probands: better reporting of stuttering in the parents because the parents themselves are providing the information and/or a higher frequency of participation by parents who themselves have a history of stuttering. A comparison of the frequencies of stuttering among siblings, conditional on whether or not either parent ever stuttered, showed no differences between the adult and child proband groups. Thus, the difference appears to be in the frequency with which families in which a parent of the proband also stutters agreed to participate in our study. This apparent bias could shift analyses toward accepting the hypothesis that stuttering is transmitted. Therefore, only adult probands have so far been used for subsequent analyses.

Among the adult probands, there were three times as many males as females. While there were more than 100 female probands, total, some of the first degree relative categories contained such small numbers as to be comparatively meaningless. Thus, female probands were eliminated in the next stage of the analyses. The data from adult male probands were divided into four categories based on whether any parent had ever stuttered. The data for siblings of these male probands are given in table 1. Analyses were done to test for transmission of stuttering using the underlying principle that if each affected individual was an independent event, then selecting for families with multiple affected would not in-

Table 1. Number of relatives (percent who ever stuttered) by parental type for male probands[1]

Parental type[2]	**N**	**F**	**M**	**B**
Number of families:	**267 families**	**65 families**	**19 families**	**5 families**
Brothers[3]				
S	58 (17.21)	24 (32.43)	6 (35.29)	2 (33.33)
NS	279	50	11	4
Total	337	74	17	6
Sisters[3]				
S	7 (2.56)	8 (10.39)	1 (5.56)	3 (37.5)
NS	266	69	17	5
Total	273	77	18	8

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[2] Parental types: N—neither parent ever stuttered; F—only father ever stuttered; M—only mother ever stuttered; B—both parents stuttered.

[3] Classifications of siblings: S—ever stuttered; NS—never stuttered.

crease the frequency of stuttering among the remaining relatives. From these data it is possible to examine whether parental stuttering affected the frequency of stuttering among the proband's siblings.

For statistical analyses only the first two categories (where neither parent stuttered or where only the father stuttered) were used. The other two categories of parental type were excluded because their numbers were too few to allow meaningful interpretations. The effect of having a father who stuttered as opposed to having no stuttering parent is quite marked and statistically significant: the frequencies of affected siblings of a proband are increased if that proband has a father who stuttered. Though the statistical analysis has no genetic hypotheses incorporated in it, this significant difference provides strong support for the hypothesis that stuttering is transmitted. What cannot be resolved by this analysis is whether the transmission is solely genetic, solely cultural, or a combination of the two.

Following these preliminary analyses, a more elaborate statistical analysis has been done on the families of all adult probands. The effects of all the variables shown to be significant were tested simultaneously using a logistic model (Cox 1970). As stated earlier, this model has some similarities to the log-linear model but uses the logistic function to estimate the frequency (θ) of affected individuals in a category as

$$\theta = \frac{e^y}{1 + e^y}$$

where y is a linear function of the parameters. Specifically, in these analyses y is the sum of an overall mean, μ, and the values associated with the specific classification criteria for the category. The classification criteria used were sex-of-proband (male or female), sex-of-relative (male or female), and parental type (neither or at-least-one parent affected). The full model includes parameters for all main classifications, three two-way interactions, and the three-way interaction. Statistical significance of a parameter estimate can be tested in two ways: by setting that parameter to zero and doing a likelihood ratio test and by testing whether the estimated value is significantly different from zero. This model is directly analogous to analysis of variance, which can also be formulated as a general linear problem. Unlike a chi-square test for association, the linear logistic model allows some inference concerning the relative magnitude and direction of the effects within a classification criterion.

The overall null hypothesis for this analysis is that any observed differences in frequencies of affected individuals among subsets of relatives are due to chance alone. This null hypothesis assumes that the subsets defined by the classification criteria are all drawn from a statistically homogeneous population. Based on the classifications used, we can define null hypotheses, rejection of which would support general hypotheses about the nature of the familial pattern present. Specific null hypotheses that would lead to a hypothesis of vertical transmission of susceptibility include:

(1) Regardless of other classification criteria applied to the relatives, parental type has no significant effect upon frequency of affected relatives of probands.

(2) Regardless of other criteria, the overall frequency of affected relatives is not different from the general population prevalence.

The results of this more comprehensive analysis for stuttering have helped define the pattern with which stuttering occurs in families (Kidd, Heimbuch, and Records 1981). A total of 294 adult male probands and 103 adult female probands and their families were studied. The samples obtained by the two methods of ascertainment were not significantly different and were pooled for this analysis. Likelihood ratio tests indicated that no interaction terms were significant. The main factors found to be significant were sex of proband, sex of relative, paternal stuttering, maternal stuttering, and type of relative. Maximum likelihood parameter estimates for the main effects are given in table 2 for the logistic model. When these parameters are used, the agreement between observed and expected frequencies of stuttering is quite good.

Next the data were examined to determine if these factors and other variables were predictors of severity of stuttering in the proband (Kidd et al. 1980). This possibility was examined using data on a subset of 184 adult stutterers and their families. Frequency of stuttering during a pretreatment oral reading task was available as the severity measure for each of these index cases and information on whether a relative ever stuttered was available on all first degree relatives. The family

Table 2. Maximum likelihood parameter estimates for main effects

Parameter	Maximum likelihood estimates: Value	Maximum likelihood estimates: Standard error
μ	−1.20	.18
a: Sex of proband		
Female	.25	.09
Male	−.25	
b: Sex of relative		
Male	.63	.09
Female	−.63	
c: Paternal stuttering		
Present	.32	.17
Absent	−.32	
d: Maternal stuttering		
Present	.35	.09
Absent	−.35	
e: Type of relative		
Sibling	−.22	.09
Child	.22	

data variables, including sex and exact relationship, combined with birth date and sex of index case were used in three types of analyses: multiple regressions, AID regressions, and stepwise regressions. None of the variables tested, including stuttering among first degree relatives, was a predictor of severity of stuttering in the index case. Apparently this measure of severity is not related to the factors which predispose to stuttering.

The next questions consider how to explain the transmission. Genetic models might be used to explain the transmission. Although stuttering does not follow a clear single gene pattern, it may very well be explained by some threshold model in which a major locus segregates three genotypes, but nongenetic variation modifies the risk of stuttering for each genotype. A threshold then determines who does and who does not stutter. We could have heterozygotes who stutter if they have a sufficiently stressful environment, and we could have homozygotes who do not stutter if they have a sufficiently benign or ameliorating environment. The position of the threshold and the gene frequencies can be varied to find the best explanation of the data. For stuttering the results are given in table 3. This solution explains the family data quite well, with the transmission having a purely genetic basis. The gene frequency in the solution is 4 percent, not a rare gene, but not a very common one either. Most individuals in the total population lack the gene. About 8 percent of the population is heterozygous, and less than 2 in 1,000 are actually homozygous. The penetrances—the probability that an individual with a particular genotype will ever stutter, as a function of sex—are virtually zero for the normal genotype; they are one (or 100 percent) for homozygotes for the stuttering allele. A striking sex difference is found for heterozygotes: penetrance is about 38 percent for a heterozygous male but only 11 percent for a

Table 3. Best fit of the single major locus model to the family incidence data on stuttering[1]

Stuttering allele (S) frequency = .040 ± .007
Predicted general incidences: .035 for males; .010 for females
Penetrances for each genotype and sex:

	Genotypes: NN	Genotypes: NS	Genotypes: SS
Male	0.005 ± 0.003	0.378 ± 0.025	1.0
Female	0.0002 ± 0.0002	0.107 ± 0.019	1.0

The goodness of fit $\chi^2_3 = 4.65$, $p = 0.22$

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heterozygous female. These parameter values predict lifetime prevalances of about 4 percent of the population of males and about 1 percent of the population of females, roughly the observed values for the lifetime prevalance of ever stuttering at some time in childhood.

Finding an acceptable solution does not constitute proof that a single locus is responsible for stuttering, but it is highly suggestive. Especially noteworthy is that the model does not require that the interaction of genetic and nongenetic factors be confined to heterozygotes and yet biological principles would suggest that genotype as the one in which that interaction is most likely to be significant. Morton and Kidd (1979) corrected for selection bias in high density pedigrees (those with five or more affected individuals) and obtained additional support for parameter estimates which closely correspond to the estimates in table 3 except that the allele frequency estimate is lower. This difference gives population frequency estimates lower than those above. The most likely gene frequency was .01 which gives population frequencies between 1.3 for males and .25 for females.

Arguing against a single major locus (SML) explanation is the finding that a multifactorial polygenic threshold model (MFP) can also explain the data (Kidd 1977). Genetic factors also account for the transmission of stuttering in the MFP model and the model also accounts for the sex differences observed. The solution gives sex-specific thresholds, with the female threshold being farther from the population mean than the threshold for males. The predicted general population incidence for males is about 5.5 percent and 1.5 percent for females with the correlation among relatives estimated at 0.38. These incidence figures correspond quite well with the observed values reported earlier, and the correlation coefficient indicates that stuttering clusters within families.

In summary, the overall pattern of occurrences of stuttering within families is definitely nonrandom. Genetic analyses of the data reveal that this pattern of stuttering can be explained by genetic transmission of susceptibility and sex-modified interaction with environment. Although the mode of transmission is not yet clearly defined, two genetic models with sex-specific thresholds closely fit the data and may help to identify the genetic nature of susceptibility to stuttering.

However, nongenetic hypotheses must also be considered before any firm conclusion can be reached. Certain models of purely cultural inheritance can be excluded by the data. The simplest cultural model—imitating the speech of a family member who stutters—could not explain more than a small fraction of all stuttering in children (Kidd, Kidd, and Records 1978). This finding is consistent with the high familial concentration of stuttering because most stutterers recover before adulthood. For example, in 20 percent of these families the father had at some time stuttered, but in one half of those cases he had recovered before the birth of the child who later stuttered. Some more complex cultural hypotheses have involved a general "nervousness" being culturally transmitted since, for example, anxiety is known to exacerbate symptoms in a stutterer. Such hypotheses predict that the severity of stuttering would be associated with the frequency of relatives who stutter. One reliable measure of the severity of stuttering is the frequency of words on which a stutterer has some difficulty. This measure of severity is *not* associated with the frequency or distribution of stuttering among relatives, and we therefore conclude that severity is not related to the transmitted factors that predispose to stuttering. Hence, hypotheses of general anxiety being the culturally transmitted cause of stuttering appear to be excluded by these data.

At this time definite proof is elusive, yet all available evidence suggests that susceptibility to stuttering is genetically transmitted.

The analysis of data on *Tourette syndrome* (Kidd, Prusoff, and Cohen 1980) is another illustration of the use of the logistic model. Several questions were addressed: Are multiple tics (MT) a milder form of Tourette syndrome (TS)? Is there a familial concentration? Is the sex difference real and not some artifact of ascertainment? If the sex difference is real, is it important in transmission?

Collection of data for this analysis has been described elsewhere (Kidd, Prusoff, and Cohen 1980). Briefly, 200 questionnaires were mailed out by the Tourette Syndrome Association (TSA) of which only 75 were returned. Followup contact with some individuals who had not returned completed questionnaires indicated a variety of reasons: questionnaire not received, individual did not have TS, etc. Of the 75 returned questionnaires, 66 included information on symptomatology on a total

Table 5. Frequency of TS and/or MT among siblings of TS patients

Type of family		Probands	
		Male	Female
Neither parent affected	Brothers	.074 ± .050 (2/27)	.400 ± .155 (4/10)
	Sisters	.043 ± .042 (1/23)	.200 ± .126 (2/10)
One or more parents affected	Brothers	.400 ± .155 (4/10)	.667 ± .272 (2/3)
	Sisters	.200 ± .126 (2/10)	.167 ± .152 (1/6)

of 231 first degree relatives in these families. Only these relatives were included in this analysis. The frequencies of TS and/or multiple tics among these relatives are shown in table 4.

Table 5 shows the data when divided into a three-way contingency table by three classifications: sex of proband, sex of sibling, and affected status of parents. The logistic model was used to test simultaneously whether each of these classification criteria resulted in statistically significant differences in the frequencies of affected siblings and whether there were any statistically meaningful interactions among these main classifications. The analyses showed that each main classification was statistically significant, but none of the interaction terms were. Therefore the values from tables 5 and 6 indicate that: (1) multiple tics appear to be a mild form of TS; (2) there is vertical transmission since the parental effect is significant; (3) the sex difference in the prevalence of TS is real; and (4) this sex difference is related to the transmission of susceptibility for either multiple tics and/or TS. Hence, a sex-modified form of transmission was demonstrated without having to assume a specific etiologic model—either genetic or cultural.

These results support previous findings which indicate that TS shows a familial concentration, especially if multiple tics are considered a minor manifestation of the trait (Eldridge et al. 1977; Shapiro et al. 1978; Nee et al. 1980). Wilson, Garron, and Klawans (1978), however, pointed out that most data purporting to show familial aggregation of multiple tics do not provide support for the hypothesis that the condition is transmitted. Most previous studies have reported only the proportion of patients with a positive family history of TS or multiple tics. Wilson, Garron, and Klawans (1978) suggest that, because the frequency of tics is approximately 10 percent in the general population, about 30 percent of patients could be expected to have a positive family history of tics (i.e., at least one affected relative) by chance alone. The conclusion reached by Kidd, Prusoff, and Cohen (1980) is that each relative has an elevated risk, thereby confirming the familial aggregation. These data suggest that, because affected status of parent (with either MT or TS) significantly affects the risk to relatives, multiple tics and TS are transmitted vertically and may have a similar etiologic base. These data also suggest that, because sex of proband (with TS) affects the risk of MT and/or TS in relatives and because opposite sex relatives are at greater risk, the transmission is sex-modified.

What these data do not do, however, is explain the cause of that transmission. While genetic models may adequately fit the data, other cultural/environmental mod-

Table 4. Frequency of TS and/or MT among 230 first-degree relatives

Type of relative	Sex of proband	
	Male	Female
Fathers	.229 ± .061	.333 ± .111
Mothers	.125 ± .048	.111 ± .074
Brothers	.162 ± .061	.462 ± .138
Sisters	.091 ± .050	.188 ± .098
Total	.157 ± .029	.262 ± .055

Table 6. The values of the parameters of the logistic model applied to family data on Tourette syndrome

Parameter	Estimated value
μ, overall "mean"	−1.25 ± .29
Sex of proband	
Male	−.66 ± .29
Female	.66 ± .29
Sex of sibling	
Male	.58 ± .30
Female	−.58 ± .30
Parental type	
Neither affected	−.66 ± .29
At least one affected	.66 ± .29

els may as well. The results reviewed here have been confirmed by additional data (Pauls et al., 1981), and therefore the patterns observed need to be incorporated into subsequent attempts to find appropriate explanations of how the trait is transmitted. For example, the sex differences need to be incorporated into both a possible genetic or environmental model.

Evaluation of these findings will require systematic investigation. Homogeneous groups identified by symptomatology, family history, response to treatment, and long-term prognosis need to be identified and studied to help in our understanding of this disorder.

Conclusion

Childhood behavioral traits are complex disorders and hence do not lend themselves to simple, straightforward genetic analyses. Methodologies are available for these kinds of traits, but the assumptions inherent in their formation often make interpretation of results difficult. There are several approaches appropriate for preliminary analyses which can help diminish the number of assumptions necessary for more complex analyses.

Data on stuttering and Tourette syndrome are examples of an approach to genetic analysis that helps identify parameters to be included in subsequent analyses. These data suggest that the two disorders are transmitted and that in both cases the transmission is sex-modified. Therefore, it is important to incorporate sex differences in subsequent analyses for these two disorders. It is also apparent that in subsequent analyses of TS, multiple tics should be considered as a milder manifestation of the trait.

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The Epidemiology of Tourette's Syndrome: A Pilot Study

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Abstract

A new, precoded, self-report questionnaire was used to collect information on 75 patient members of the Tourette Syndrome Association. This diverse group of Tourette's syndrome (TS) patients supplied by mail detailed medical, symptom, developmental, family, and personal history information. Analysis of these data supported the usefulness and validity of the questionnaire, and also indicated that the diagnosis of TS is being made earlier; attentional difficulties may be basic to the disorder; haloperidol is an effective treatment for many patients, but alternative treatments are needed because unpleasant side effects of haloperidol often lead to discontinued use, and TS is disabling for many with most patients reporting serious problems in one or more areas of functioning.

In 1885, Gilles de la Tourette vividly described a neuropsychiatric syndrome with a unique constellation of clinical features: multiple motor tics, phonic symptoms, compulsions, and other behavioral phenomena, such as the irresistable urge to echo or imitate. He observed its predominance in males, early onset, and lifelong duration, and speculated that its cause might lie in perhaps inherited neurological vulnerability. Following Tourette's report, with increasing frequency in the past 20 years, hundreds of cases and series of patients have been described in the world literature, leaving little doubt that Tourette's syndrome (TS) is a clinically recognizable disorder with a stable pattern of expression across cultures (Abuzzahab and Anderson 1973; Shapiro et al. 1978). While each patient presents his own set and pattern of symptoms, there is a remarkable similarity in clinical phenomenology and natural history, with a waxing and waning course in which symptoms disappear and are replaced by new ones.

Tourette's syndrome was once thought to be a rare clinical curiosity. However, the discovery of the therapeutic value of haloperidol in the mid-1960s (Shapiro and Shapiro 1968), and the exceptional public information campaigns of the national Tourette Syndrome Association have led to increasing recognition of the disorder and more frequent, earlier diagnosis (Shapiro et al. 1978). During the past decade, the use of new biochemical strategies in the study and treatment of TS and other neuropsychiatric disorders (van Woert et al. 1976; Cohen et al. 1978; Friedhoff and Alpert 1978; Cohen et al. 1979*a*) has generated increasing interest in the possible neurochemical basis and correlates of TS. This new research requires more refined understanding of the clinical characteristics of TS in large, representative populations of patients.

To a remarkable extent, research on TS has been facilitated by the Tourette Syndrome Association (Lake et al. 1977; Wassman et al. 1978), and the present study was undertaken in collaboration with them. Access to this national group (whose registry includes nearly 2,000 purported TS patients) afforded us the opportunity

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to study a geographic, racial, and ethnic cross-section of TS patients. In this article, we present the results of a pilot study, which employed our newly developed Tourette's Syndrome Questionnaire (TSQ). The pilot study objectives were to gather systematically a spectrum of information on TS patients and to assess the usefulness and validity of the TSQ. Concurrently, the TSQ was used with a clinically diagnosed population of TS patients which supported its validity; the results of the clinical project have been reported separately (Cohen et al. 1979*b*).

Methods

Questionnaire Design. The precoded, self-report TSQ was designed to elicit a patient's detailed medical history and clinical picture in the context of the individual's social and psychological development and personal experiences. The questions contained in the 35 pages of the TSQ are categorized and arranged under the following subject headings: Patient Personal Data Inventory; General Medical History; History of Tourette Symptomatology; Treatment History; Family History; Prenatal and Birth History; and Developmental History. The patient's mother was requested to complete the birth and prenatal history questions, and parents were asked to assist with the developmental and family history questions. However, the entire questionnaire may have been completed by or with the assistance of the patient's parents. Content of the questions was based on numerous sources including patient interviews, Tourette Syndrome Association member suggestions, literature reports, and contributions from researchers and clinicians in the fields of child psychiatry, psychology, neuropharmacology, epidemiology, and genetics.

Subjects. Ten percent of the Tourette Syndrome Association patient membership was selected for the questionnaire survey by a systematic sampling technique on an alphabetic file. Anonymity of respondents was ensured by a numerical identification system controlled by the Tourette Syndrome Association (TSA). Questionnaires were mailed to the 200 selected patients. A followup letter was sent to nonrespondents. The TSA contacted those who had still not responded by telephone to encourage response, to assess reasons for failure to respond, and to determine characteristics of nonresponders.

Results

Response Rate. After the initial mailing, 61 completed questionnaires were returned. Three more were returned after the followup letter, and an additional 11 after the telephone survey, bringing the total to 75 completed questionnaires (37.5 percent of those sent).

Of the 136 initial nonresponders, only 36 (26 percent) were reached by telephone. Among those, seven stated that they did not have Tourette syndrome; six reported that they had never been formally diagnosed, but believed they had TS. Twenty-one stated that they had been formally diagnosed as having TS, and 11 of those patients subsequently returned questionnaires. Reasons given for nonresponse included: lost or did not receive questionnaire (28 percent); were not interested in the questionnaire (22 percent); felt unable to complete the questionnaire (19 percent); did not have Tourette syndrome (11 percent); believed the questionnaire to be too long (8 percent); and felt the questionnaire to be an invasion of privacy (6 percent). Six percent of those contacted offered no reason for not completing the questionnaire.

Demographic Findings. Fifty-seven of the respondents were male (76 percent), and 18 (24 percent) were female. Ages of the patients ranged from 8 to 57 years of age: 28 percent were 12 years or younger, 37 percent were 13 through 19, and 35 percent were 20 or over. All but two of the patients were white; one black and one oriental patient responded. Of the patients 18 years of age or older, 33 percent were married, 53 percent were single, and 14 percent were separated or divorced. The educational level of patient households was high: Among patients living with parents, 60 percent of the heads of household had at least some college. Thirty-eight percent of the patients were in Hollingshead's (1965) social class III, 16 percent in I, 19 percent in II, 19 percent in IV, and 7 percent in V (mean social class 2.8).

General Medical History. Patients reported having had a variety of common childhood illnesses, but in the absence of a control group no statistical evaluation was possible. No marked frequency of an unusual disease was noted.

Medical Disorders and Tourette Syndrome Onset. Thirty-six percent of the patients indicated that a specific medical problem immediately preceded and may have been associated with the onset of TS symptoms. However, the problems cited were thinly distributed among such diverse "precipitators" as rheumatic fever, head injury, respiratory disorder, measles, digestive disorder, and use of a drug.

Onset and Diagnosis. The first signs of TS were noticed by family members as early as 2 years and as late as 16 years of age, with a mean of 7 years of age. The average interval between the onset of symptoms and the determination of a TS diagnosis was 7.6 years. Younger patients, those under 21 years of age, reported a considerably shorter period between onset and diagnosis (3.5 years) than did older patients (15.5 years). Based on their TS symptoms, 39 percent of the patients had been assigned one diagosis other than TS, and 45 percent had been given two or more different diagnoses. Only 16 percent received a Tourette's syndrome diagnosis the first time they were diagnosed. The most frequent of the other diagnoses reported were emotional problems, transient tics of childhood, chorea, hyperactivity, "nervousness," and residual effects of a physical illness. Most patients were told they had TS by either a neurologist (60 percent) or a psychiarist (32 percent).

More than half of the patients (51 percent) first suspected that their disorder was TS after hearing about TS from the mass media, while only 40 percent were first alerted by a physician. The most common first symptom noticed by family members or others was reported to be a tic of the eyes or face (57 percent); other much less frequent first signs included tics of the extremities and trunk, and a variety of vocal tics and compulsive actions.

Symptomatology. In order to ascertain the ages at which a number of symptoms first appear, patients were asked to indicate when (or if) each of 23 symptoms listed was first experienced. (See table 1 for the symptoms as they appeared on the questionnaire, and the number and percentage of patients who "ever" experienced each of them.) Space was provided for additional symptoms not included on the list. Patients reported a virtually inexhaustible variety of tics and other symptoms, and because it often was not productive to consider each separately, we will report symptom findings in three broad categories: (1) motor tics, (2) vocal tics, and (3) compulsive actions.

Motor tics of the eyes, face, and head were reported to have occurred earliest (mean 7.2 years). In addition, more patients (95 percent) reported having had these tics than any other symptom. Consistent with the description by Mahler, Luke, and Daltroff (1945) of the progression of symptoms over time, our findings suggest a cephalo-caudal sequence in the development of motor tics with the following mean ages of onset recorded: eyes, face, or head (7.2 years); shoulder or neck (8.7 years); arms or hands (9.1 years); trunk (9.5 years); and legs (10.1 years). While the symptom progression appeared to be continuous, the differences in mean ages were slight and significance levels for these differences have not been determined. (Figure 1 graphically displays the ages of onset of these and other symptoms.) It should be noted that these are means and that not all patients experienced each motor tic in turn, if at all. Additional analyses of within-patient onset data are needed to confirm the symptom progression found across patients.

When viewed as a group of symptoms, motor tics first appear at an earlier mean age (8.7 years) than either vocal tics (10.7 years) or compulsive actions (10.8 years). Of particular interest to patients is the finding that 37 percent of the patients in our sample claimed to have had coprolalia. However, since the mean age of first occurrence was 11.1 years, it is possible that the younger patients in our sample who had not had the symptom will have it in the future. The most frequent vocal tic was the uttering of low noises (84 percent of the patients).

Fewer patients claimed to demonstrate compulsive actions than either motor or vocal tics. The most frequent compulsive action was that of touching objects (55 percent of the patients). Touching of sexual organs of self or others was reported by 36 percent of the patients, with a mean onset age of 11.7. Self-destructive behaviors were serious problems for some patients; 12 percent reported biting themselves and 17 percent reported that they banged their heads.

One-fourth of the patients indicated that they had experienced an internal tic, that is, one they feel but do not express. One-third stated that they presently feel they have tics more on one side of the body than the other; however, neither side was systematically favored.

Seventy-one percent of the pa-

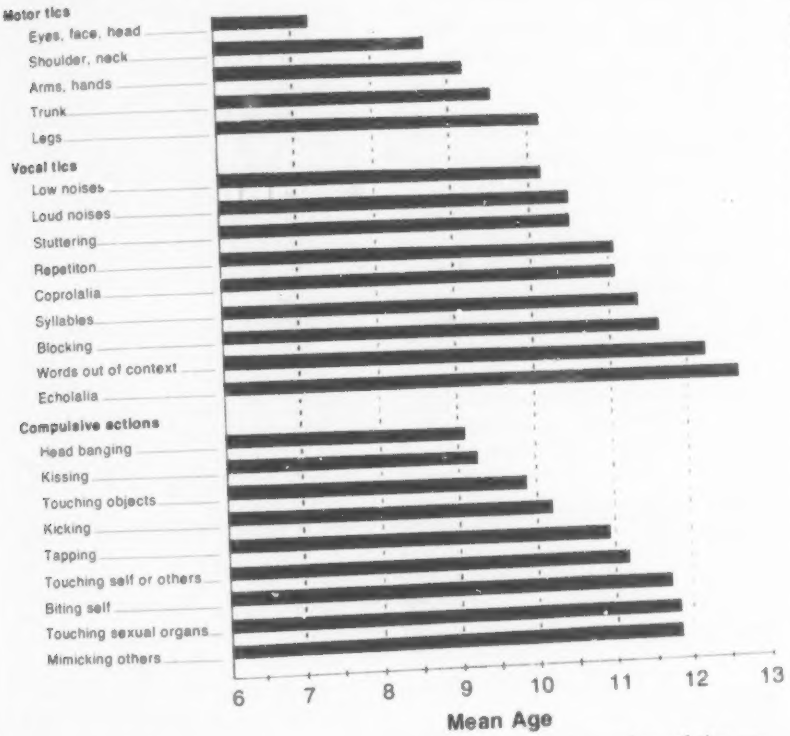
Table 1. Symptom abatement across patients ($n = 75$)

Symptom	Patients ever experiencing		Patients ever experienced who are not now experiencing	
	Number	Percent	Number	Percent
Motor tics				
Eyes, face, or head	71	94.7	7	10.0
Shoulder or neck	69	92.0	18	26.1
Arms or hands	62	82.7	12	19.4
Trunk	46	61.3	9	19.6
Legs	46	61.3	16	34.8
Vocal tics				
Low noises	63	84.0	16	25.4
Loud noises	50	66.7	22	44.0
Syllables	20	26.7	8	40.0
Words (out of context)	22	29.3	3	13.6
Repetition	41	54.7	16	39.0
Echolalia	28	37.3	12	42.9
Stuttering	20	26.7	3	15.0
Blocking	28	37.3	4	14.3
Coprolalia	28	37.3	7	25.0
Compulsive actions				
Touching objects	41	54.7	6	14.6
Touching self or others	39	52.0	9	23.1
Mimicking others physically	16	21.3	7	43.8
Tapping	32	42.7	8	25.0
Kicking	27	36.0	10	37.0
Kissing	11	14.7	1	9.1
Touching sexual organs, self, or others	27	36.0	7	25.9
Biting self	9	12.0	2	22.2
Head banging	13	17.3	7	53.8

tients claimed that certain parts of the body currently were affected more severely by TS symptoms. The eyes, face, and head were named by 62 percent, the arms or hands by 21 percent, and the shoulders or neck by 13 percent. When patients were asked to rate the relative severity of 23 symptoms listed, which they currently were experiencing, no symptom was rated consistently as more severe than the others on the list. The mean severity of most symptoms ranged from mild to moderate. Several patients wrote in and rated the severity of symptoms which did not appear on our list, but in many cases the symptom that they specified was an example of one of the 23 symptoms listed. Some of the exceptions were turning in circles while standing or walking, sniffing objects or people; smelling fingers; mouthing, but not uttering, obscene words; spitting; pulling hair; irregular breathing patterns; mouthing objects; rocking self to sleep; and hitting self. The severity of these "other" symptoms was rated as slightly greater than those symptoms that were presented on our list. However, most of the "other" symptoms were mentioned by only one patient, and that patient may well have specified the symptom because it was severe or particularly troublesome.

The current severity question allowed us to compute the number of patients currently experiencing each symptom, and the number of symptoms currently being experienced by patients by age. Motor tics were reported most frequently (95 percent of the patients currently were experiencing one or more),

Figure 1. Mean age of occurrence of Tourette tics



with tics of the eyes or face currently being experienced by 85 percent of the patients, tics of the shoulders or neck by 68 percent, tics of the arms or hands by 67 percent, and tics of the trunk by 50 percent. Seventy-six percent of the patients currently were experiencing one or more vocal tics, and the uttering of low noises was the most frequently cited among them (63 percent of the patients). Compulsive actions were experienced currently by two-thirds of the patients; the most common compulsive action was touching objects (47 percent of the patients). Statistical analysis revealed no significant age differences in the type (motor tics, vocal tics, or compulsive actions) or number of tics reported as currently being experienced by patients.

Changes in Symptomatology. Fifty-two (69 percent) of the patients had experienced a period of time greater than 1 week during which symptoms were greatly reduced or disappeared entirely. Among 41 patients who described at least one such period, 24 (59 percent) were taking medication at the time and 17 (41 percent) were not.

Further, an examination of whether a patient who had ever experienced a particular symptom was currently experiencing the symptoms revealed that specific symptoms disappear slightly more often when patients are on medication but not significantly so. Table 1 presents the number and percentage of patients who ever experienced each symptom and the number and percentage of patients who had no longer had each symptom. Percentages of patients who no longer had a symptom ranged from a high of 54 percent (patients who once experienced head banging but did not at the time they were surveyed) to a low of 9 percent (patients who once experienced kissing but did not at the time they were surveyed), indicating that some symptoms were much more likely to abate than others. However, this did not appear to be related to the commonality of the symptom (e.g., motor tics of eyes, face, or head) or type of symptom (e.g., motor tic, vocal tic, or compulsive action).

Patients were requested to indicate how each of a number of situations affected their symptoms—that is, whether the situation did not affect symptoms, increased symptoms, or decreased symptoms. The general inconsistency of responses indicated marked differences in the reactions of individual patients to most situations. However, relative agreement among patients was noted for four situations: Symptoms increased during emotional trauma, when patients were fatigued, and when upset or anxious; symptoms decreased only during sleep.

Clinical Procedures. Patients reported undergoing a variety of clinical procedures. Seventy-three percent of the patients had been treated by either a psychiatrist or a psychologist for TS symptoms. Although only 16 percent felt that this treatment had helped in reducing symptoms, 38 percent did believe that it had helped them cope with their symptoms. Twenty-seven percent of patients treated by a psychiatrist or psychologist had undergone psychotherapy or psychoanalysis, and the majority of them (75 percent) felt it had neither a positive nor a negative effect. A small number of patients had undergone behavior modification (12), hypnosis (9), physical therapy (5), or treatment by a chiropractor (10), and in each of these cases at least two-thirds believed that there was no beneficial effect. The one patient who had undergone electroshock therapy believed that the treatment had been harmful.

Electroencephalographic (EEG) Results. Sixty-two (83 percent) of the patients had had at least one EEG done. Of these, 58 percent reported a normal result on their most recent EEG, 11 percent reported a borderline result, and only 8 percent a clearly abnormal result; 19 percent did not know the result of their EEGs. Three patients failed to report their most recent EEG results.

Pharmacotherapy. Fifty-one (68 percent) of the patients indicated that they currently were taking medication for their TS symptoms; forty-six (63 percent) of the patients currently were taking haloperidol. The nature of the questionnaire did not enable us to determine the medication currently taken by the remaining five patients.

Since haloperidol has been the drug of choice for the treatment of TS, the patterns of characteristics of haloperidol usage among the patients sampled were assessed. Sixty-eight (91 percent) of the patients in our sample had taken haloperidol at some time (for a mean duration of 31 months), and 88 percent of those patients had experienced a reduction in symptoms. Of the patients who experienced a reduction in symptoms, 43 percent felt that their symptom reduction was uniform and not symptom-specific, while 50 percent stated that certain symptoms were helped more than others. The symptoms that patients cited as being helped more varied widely, but motor tics were mentioned slightly more frequently than other symptoms.

One or more undesirable side effects were noted by 80 percent of the patients who had ever taken haloperidol, with lethargy, impaired functioning, and depression accounting for the majority (60 percent) of the complaints (see table 2). Twenty (29 percent) of the patients who had ever taken haloperidol stopped taking it. The majority (80 percent) had discontinued use because of unpleasant side effects. Only two patients (10 percent of those who stopped) had stopped because haloperidol had been ineffective in treating symptoms.

Patients were asked to indicate on a list of other drugs those that they had taken in the past and whether those drugs had had a good or bad effect on their TS symptoms. For most drugs listed,

Table 2. Unpleasant side effects experienced by patients taking haloperidol

Side effect	Number reporting side effect ($n = 63$)[1]	Percent of those responding to question
None	8	12.7
Lethargy	34	54.0
Impaired functioning	17	27.0
Depression	7	11.1
Parkinsonian symptoms	9	14.3
Weight gain	5	7.9
Impaired motor control	2	3.2
Restlessness	2	3.2
Headache	1	1.6
Slurred speech	1	1.6
Repetition of words	1	1.6
Loss of memory	1	1.6
Schizophrenic behavior	1	1.6
Numbness of tongue	1	1.6
Facial paralysis	1	1.6
Frequent urination	1	1.6
Got "high"	1	1.6
Drowsiness	1	1.6

[1] Side effects are not mutually exclusive. Some patients reported as many as three side effects. Sixty-eight patients had taken haloperidol at some time, but only 63 responded to this question.

patients noticed no effect on their symptoms. Exceptions for which a "good effect" was reported as frequently or more frequently than "no effect" were diazepam (45 percent) and benztropine mesylate (57 percent). A "bad effect" was reported as frequently or more frequently than "no effect" for phenytoin sodium (50 percent), methylphenidate hydrochloride (57 percent), and amphetamine derivatives (71 percent).

Haloperidol Usage and Symptom Presence. As mentioned above, most (92 percent) of the patients who were currently taking medication for their TS symptoms were taking haloperidol. We compared patients taking haloperidol with patients not taking it to see if the groups differed with regard to specific symptoms ever experienced that were "not" now experienced. There was a trend for patients taking haloperidol to have lost specific symptoms more than those not taking haloperidol, but there were no significant differences between the groups. It should be kept in mind that this analysis was based on the presence/absence of symptoms and not on the relative severity or frequency of a symptom or symptoms.

Family History. One section of the questionnaire dealt with the family history of TS and/or multiple tics. Each respondent was asked about all of his first-degree relatives (parents, siblings, children), his spouse, his aunts and uncles (by specific relationship), and his half-siblings (specifying shared parent for each). The information solicited on each relative was (1) whether that relative had ever had TS and (2) whether that relative had ever had multiple tics. Responses were "no," "yes," and "don't know."

Analysis of these data on parents and siblings of the TS patient disclosed that in families of TS patients the syndrome of multiple tics occurs more frequently in male than in female relatives. This finding offers a possible explanation for the preponderance of male patients in our sample. Further, our analysis revealed that the sex difference is related to the genetic transmission of susceptibility to TS. The complete results of this analysis are described elsewhere (Kidd, Prusoff, and Cohen 1980).

Prenatal and Birth History. Sixty-seven mothers of the patients surveyed completed this section of the questionnaire. These data have not been compared to similar data obtained from a control population, but the preliminary analysis found little out of the ordinary that would warrant such a comparison study.

Infancy and Early Childhood. The reported early development of the patients in our sample was unremarkable. During the first month of life they were active and strong (97 percent) and attentive to sights and sounds (100 percent). Developmental landmarks were achieved relatively early by most patients: 73 percent sat without assistance at 6 months or younger; 52 percent said words by 10 months and 92 percent by 17 months; walking began by 11 months for 43 percent and by 13 months for 85 percent. Ninety-two percent of the patients completed bowel and urinary training by about 3 years of age. The most frequently noted behavioral problems when patients were between 1 and 5 were sleeping problems (32 percent), being difficult to manage (27 percent), bladder and bowel problems (25 percent), and unusual fears (24 percent).

Ages 5 to 12. Enuresis was a problem for 27 percent of the patients beyond the age of 5, for 19 percent past age 6, and for 11 percent past age 9. Parent assessment of patient school performance from ages 5 through 12 indicated that similar numbers of patients were judged to have achieved at below average, average, and above-average levels in arithmetic, writing, and spelling. However, 51 percent of the respondents felt that the patient's school performance was not what it should have been. Thirteen percent of the patients had been kept back in school, and 6 percent had been advanced a grade sometime during this age period.

Classroom and learning difficulties when patients were between the ages 5 to 12 were frequently cited. Sixty-nine percent reported that teachers had complained of listening and attention problems, and parents of 50 percent of the patients concurred with this assessment. Forty-two percent of the patients had had teachers say that they were hard to control in the classroom. It should be noted that the following were not mutually exclusive: twenty-seven percent of the patients had been placed in special classes, 21 percent had been assigned a special teacher, and 19 percent had been diagnosed as having a learning disability. Forty percent of the patients were judged to be more awkward and clumsier than other children in the 5 to 12 age bracket. Twenty-five percent of the patients had been diagnosed hyperactive by a physician between the ages of 1 and 11, and 12 percent were diagnosed as having minimal brain dysfunction (MBD) between the ages of 5 and 12; some patients had received both diagnoses at different times.

The social stigma of TS at these ages was evidenced by the high percentage (75 percent) of patients who were teased about their symptoms by classmates. However, 72 percent of the patients stated that they had had a best friend when they were between the ages of 5 and 12, and 92 percent had some friends.

Ages 12 to 18. Between the ages of 12 and 18, patients again were distributed similarly in below-average, average, and above-average groups for arithmetic, writing, and spelling. However, respondents reported that for 66 percent of the patients, school performance was not what it should have been compared with 51 percent judged to be performing below ability from ages 5 to 12. Fewer patients were said to have been hard to control in the classroom between ages 12 and 18 (27 percent) than between ages 5 and 12 (42 percent). Listening and attention continued to be problems for patients between ages 12 and 18 (49 percent). Thirty-one percent of the patients were in special classes and 22 percent were assigned a special teacher during this age period. Thirty-five percent of patients were reported to be more awkward or clumsier than others between the ages of 12 and 18. However, 83 percent participated in sports, and of those participating, 79 percent were considered to be at least average athletes.

Seventy-seven percent of the patients reported that they had had a best friend, and 51 percent had dated when they were between the ages of 12 and 18. Virtually all (98 percent) of the patients had some friends, but 73 percent had been teased by peers about TS symptoms at these ages. Forty-eight percent of the patients felt that teachers had been unfair or difficult to deal with, and 23 percent reported that they had been teased or ridiculed by teachers about TS symptoms.

Other Developmental Findings. Fifty-six percent of the patients were reported to be above average in overall intelligence, and 41 percent were average. Questions concerning patient handedness revealed that 82 percent were right handed and 17 percent left handed. No patient reported having been forced to change handedness. There were no unusual findings concerning age of onset of puberty.

Emotional Status. Sixty-seven percent of the patients had seen a mental health professional for emotional or psychological problems; 13 percent had been hospitalized for psychiatric reasons. Off medication, the aggressiveness of the patients in our sample was reported to be above average for 39 percent of the patients, average for 32 percent, and below average for 29 percent. Patients' sensitivity to pain off medication was considered to be normal for 54 percent of the patients, above average for 29 percent, and below average for 16 percent.

Effects on Family Relationships. Forty percent of the patients with siblings felt that their relationships with brothers and sisters were affected for the worse by TS, but the majority (58 percent) felt that these relationships were not affected at all. The relationships between patients and parents were found to be affected slightly more often, with 50 percent claiming that the relationship was affected for the worse and 46 percent not at all.

Effects on Social Contact. As can be seen in table 3, when patients were asked how the quality of their social contact was affected by TS, 12 percent claimed not at all, 32 percent only a little, 30 percent

Table 3. Degree to which Tourette syndrome affects patients' social contact, school performance, and job performance

Degree affected	Social contact outside family (percent)	School performance (percent)	Job performance (percent)
Not at all	11.6	15.1	29.6
Only a little	31.9	32.1	37.0
Moderately	30.4	20.8	11.1
Substantially	14.5	20.8	14.8
Severely	11.6	11.3	7.4
Number responding	$n = 69$	$n = 53$	$n = 27$

moderately, 14 percent substantially, and 12 percent severely.

Effects on School and Job Performance. Among student patients, school performance was not felt to be affected by 15 percent, was felt to be affected only a little by 32 percent, moderately by 21 percent, substantially by 21 percent, and severely by 11 percent. Among patients with full-time occupations, 30 percent felt their job performance was not affected by TS, 37 percent that it was slightly affected, 11 percent moderately, 15 percent substantially, and 7 percent felt that their job performance was severely affected (see table 3).

Specific Difficulties Encountered by TS Patients. Patients were asked to respond to questions concerning specific difficulties they have faced. Among those who had the necessary experience to respond to each question, 14 percent encountered difficulties in obtaining health insurance, 13 percent in obtaining life insurance, 13 percent in obtaining a driver's license, 25 percent in obtaining employment, 34 percent in holding a job, and 9 percent in gaining admission to college or other higher education (see table 4).

Patient Attitude Toward Having TS. When patients were asked to characterize their current attitude toward having TS (table 5), 16 percent said that they felt like an average person, 49 percent said that TS is a problem but one they face as a challenge, 24 percent said that it is a serious problem but that they compensate when possible, and 10 percent that they had serious shortcomings and were pessimistic about the future.

Table 4. Percentage of patients experiencing specific difficulties as a result of Tourette syndrome

Area of difficulty	Percent experiencing difficulty	Number responding
Obtaining health insurance	13.9	36
Obtaining life insurance	12.9	31
Obtaining a driver's license	13.3	30
Obtaining employment	25.0	28
Holding a job	34.5	29
Gaining admission to higher education	8.7	23

Table 5. Patient attitude toward having Tourette syndrome ($n = 67$)

Attitude	Percent
Feels like an average person	16.4
Is a problem but faces it as a challenge	49.3
Is a serious problem but compensates when possible	23.9
Feels serious shortcomings, is pessimistic about the future	10.5
Withdrawn, ashamed, overcome	0

Discussion

The major objective of this study was to gather a broad spectrum of information on TS patients. The low (37.5 percent) response rate to our pilot survey was disappointing; nevertheless, our sample comprises a diverse group of TS patients. While response to the questionnaire may have been related to the demographic characteristics of the sample, there is no reason to believe that nonresponse was related to the history, symptomatology, or treatment of the disorder.

Validation of the TSQ. Both the literature and our clinical experience support the usefulness and validity of the TSQ. Indeed, our survey findings are remarkably similar to those reported (Shapiro et al. 1978; Abuzzahab and Anderson 1973; Nee et al. 1980) and our clinical project findings (Cohen et al. 1980), namely: the 3.2:1 male to female ratio; the age of onset between 2 and 16 years, with a mean of 7 years; the suggestion of a cephalo-caudal sequence in the development of motor tics; overall symptomatology and course; treatment history; and genetic susceptibility to TS.

Diagnosis of TS. While any delay in the diagnosis of TS can lead to unnecessary bewilderment and inappropriate treatment, our data show that patients now are likely to go undiagnosed for much shorter periods. However, most patients had been assigned at least one diagnosis other than TS. Insidious onset and clinicians' lack of experience with TS may account for some of the "misdiagnosis" (e.g., transient tics of childhood and chorea), but in other cases patients may well have met the criteria for the diagnosis assigned them. For example, a number of patients had been diagnosed hyperactive, with a learning disability, or with minimal brain dysfunction (MBD)—diagnoses which do not share essential criteria with TS, but which have been associated with it (Moldofsky, Tullis, and Lamon 1974; Shapiro et al. 1978). The *DSM-III* (American Psychiatric Association 1980) recognizes that a patient may meet criteria for more than one disorder and provides for multiple Axis I and II diagnoses. For the TS patient, concomitant diagnoses are of particular value in the implementation of a therapeutic program (e.g., special education). Further research is needed to delineate the relationships between the diagnostic criteria for TS and other disorders that appear frequently in association with it.

Subgroups of Patients. The TSQ and the clinical data support the notion of heterogeneity, on clinical and genetic grounds, among TS patients. However, whether there is currently any strong evidence for this heterogeneity having clinical or biological implications is not known. We do not yet know if there are important biological or therapeutic response differences between patients with or without coprolalia, with or without family history, or with or without EEG abnormalities. To determine the meaning of these within-diagnosis differences, future research should use increasingly refined typologies including family history, symptom pattern, associated or other diagnoses, and response to medication.

EEG Results. Eighty-three percent of the patients had had at least one EEG; of these, only 11 percent reported a borderline result and 8 percent a clearly abnormal result. Since physicians tend to minimize EEG results to patients, and since a large number of the patients (19 percent) did not know the results of their EEGs, these findings may represent an underreporting of the actual incidence of borderline and abnormal EEGs among the patients in this sample.

Haloperidol Usage. Our data show that haloperidol is effective in the treatment of TS and is useful for some patients for whom side effects are minimal and the therapeutic gains worth the inconvenience they may experience. The fact that haloperidol was thought to be the "magic cure" for TS has held up research into other possible treatments and, clearly, for many of the patients in our sample alternatives are needed.

Effects of TS on Patient Functioning. Patient responses to a number of questions regarding the effects of TS on their attitudes toward life, school, and job performances, family and social relationships, and other areas of functioning revealed that some patients are remarkably optimistic about the future and have managed to maintain "normal" lives in spite of TS. However, our data suggest that TS has caused serious problems for a majority of patients and has been debilitating for many. The reported differences in patient attitudes and patient functioning may reflect actual differences in the severity of their symptoms. In addition, the fact that symptoms had disappeared or were greatly reduced for at least one period lasting 1 week or more (reported by 69 percent of the patients) may have contributed to the optimism expressed by some patients.

School and Work Problems. Ninety-seven percent of the patients in our sample were reported to be of average or above-average intelligence, yet the majority of them reported school and attentional difficulties. Many had required special educational provisions. A number of patients had had difficulty obtaining and/or holding a job, and among those with full-time occupations, one-third claimed that their job performance was moderately to severely affected by TS. On the basis of these data and our clinical findings, we believe that these reported school- and work-related problems are due not only to the limitations imposed by TS symptoms, e.g., noises and compulsions, but also to basic attentional difficulties, which may be exacerbated by medication side effects.

Social and Family Relationships. Most respondents reported that social and/or family relationships were negatively affected by TS. Three-quarters had been teased by peers, nearly half had found teachers unfair or difficult to deal with, and nearly one-fourth had been teased or ridiculed by teachers. Social contact was reported to be moderately to severely affected by more than half of the patients. While TS would seem to strain family relationships, many patients felt that relationships with siblings and parents had not been affected at all by their disorder.

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The **Ninth World Congress of Social Psychiatry** will be held in **Paris, France, July 5–9, 1982**. The Congress is being organized by L'Association Française de Psychiatrie et de Psychopathologie Sociales (President of the Congress: P. Jean; President of the Scientific Council: P. Sivadon). Its main aims are:

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- To provide a forum for discussion among representatives of different cultures and all professionals concerned with the mental health field.

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Communication Development and Its Disorders: A Psycholinguistic Perspective

by Rhea Paul and Donald J. Cohen

Abstract

There is a reciprocal relationship between the study of language disorders and research in normal language development. Recent studies in normal acquisition have led to a model of language development that includes not only linguistic achievements, but the development of social and cognitive abilities that lay the basis for the transition from prelinguistic communication to the use of conventional forms. This model has been applied to the study of developmental disorders of language learning. Such a model allows the more puzzling disorders of language development, such as childhood aphasia and primary autism, to be placed in a framework that predicts language disruption when underlying perceptual, cognitive, or social abilities are lacking. Assessment procedures that can be drawn from the model of language disorders are presented. It is argued that the study of these disabilities is important in the building of theoretical models of intact language processing that specify more precisely the contribution of underlying skills to overall functioning. Questions for future research that serve this reciprocal purpose are discussed.

One of the most frequent presenting problems in children referred for developmental disorders of any kind is a delay in the acquisition of language. Failure to talk at the appropriate age may be the first signal that alerts parents to the fact that their child is different from other children, or it may be the culmination of a long period of vague suspicion that there is something "funny" about the child. In both cases, it is very often the child's lack of speech that finally impels the parents to seek professional help.

Psycholinguistic research into these failures in language acquisition has been of interest not only to those who deal with communicatively impaired youngsters, but also to theorists concerned with the nature of language and the normal course of its development (Itard 1806; Jakobson 1968; Lane 1976). Disorders of language learning have been seen as "natural experiments" in which the usually integrated components of communicative function—motoric, perceptual, intellectual, affective, interactional, and linguistic—can be "teased" apart so that the effect of disruption of one aspect of the system on the others can be seen. In this way, the examination of language disorders has contributed to theoretical models of intact linguistic processing and to the understanding of the complex relations among the biological, psychological, and social forces that result in the normal child's remarkable and apparently effortless facility for picking up language.

At the same time, recent years have seen a tremendous increase in interest in normal language development on the part of clinicians and investigators who work with communicatively impaired children. One reason for this interest is the current explosion in the literature on language acquisition, which was sparked by Chomsky's (1957) formulation of a transformational grammar, a powerful theor-

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etical model of the structure of human language. Transformational grammar influenced linguists' conception of their subject in many ways, but it also provided psychologists with testable hypotheses about, for example, the relative complexity of syntactic structures. These hypotheses could be examined by looking at the order of acquisition of these structures during the developmental period. Although transformational notions were eventually abandoned because they failed to take into account either the semantic limitations or the nonverbal communicative bases of early language, nonetheless they played an important role in kindling an intense interest in language acquisition among psychologists. These researchers have collected a wealth of information about the course of communication development and have made important changes in the way it is understood.

The accumulation and dissemination of this information has given rise to a second reason for interest in normal development on the part of clinicians. Understanding more about the nature of language learning has led to a growing conviction that the normal sequence provides the best curriculum guide for teaching language and communication skills to children who have not, for one reason or another, managed to learn them on their own (Lee 1974; Miller and Yoder 1974; Tyack and Gotsleben 1974; Bloom and Lahey 1978; Naremore 1980; Miller 1981). As a result of these mutual concerns, a reciprocal relationship has been established between clinicians and psycholinguists. Clinicians' skilled observations of children with disorders provide data for psycholinguists to use in constructing theories of the acquisition of language and its role in development, while new data and theoretical formulations on the normal course of language learning give clinicians additional categories for organizing their observations and rationales for designing intervention strategies.

For this reason, it is useful to review what has been learned about the development of communication and to follow the shifts in focus that this research has taken. In this way, it will be possible to formulate the questions for future research that will be of the greatest interest not only for the study of clinical populations, but also for the understanding of the normal child's ability to learn to communicate through language.

Communication Development in Normal Children

The Neonate's Equipment for Language Learning. How is the newborn biologically organized to make use of the linguistic environment that must eventually be assimilated? Certain perceptual abilities appear to be present from the first weeks of life, including special responsiveness to sounds in the frequency range of the human voice (Hutt et al. 1968), a preference for speech over other rhythmic sounds (Butterfield and Siperstein 1974), and a tendency to synchronize movements with pauses in speech (Condon and Sander 1974). In addition, infants as young as 4 weeks of age have been shown to be able to make categorical distinctions between phoneme pairs, such as /b/ and /p/ (Eimas et al. 1971). It seems, then, that the infant comes to the task of learning language with attentional mechanisms that favor linguistic stimulation and auditory equipment capable of imposing structure on it. This apparently innate organization is not limited to auditory processing, however. As Bornstein (1975) shows, infants divide the visual spectrum, as well, into adult categories, i.e., blue, green, yellow, and red.

Infants also exhibit well-organized social behavior in their first months. Looking, smiling, and vocalizing are put to use by young infants in securing and maintaining caregivers' attention (Ainsworth, Bell, and Stayton 1974). Infants also show early preferences for human faces over other visual stimuli (Fantz 1961, 1963, 1966; Kagan and Lewis 1965). These very early propensities for human interaction will certainly help bond babies to caregivers to ensure the nurturance necessary for survival, as Freedman (1974) suggests. But, in addition, they provide frames for increasingly complex communication routines which will eventually include conventional grammatical communication through language.

Thus, infants begin life with not only attentional preferences for human, linguistic stimulation, but also with social behaviors that can elicit this stimulation. In addition, they impose perceptual structure upon the events they experience. These abilities derive from a set of innate, "hard-wired" systems for processing sensory input. The existence of built-in systems such as these provides enormous economy to the task of learning language. Knowledge of their existence must also lead to questions about their role in later development. To what extent might these early attentional, perceptual, and social capacities be impaired in language-disordered youngsters? How will their impairment impede later language learning? How can detection of these early deficits improve treatment strategies?

"Conversation" in the First Year of Life. Bruner (1974) has described the role of mother-infant interaction in the "ontogenesis of speech acts." Proto-conversational exchanges between caretakers and babies occur in the context of mutual gaze that is coordinated with interactive vocalizations. Infants and their caretakers look at each other and take turns babbling sounds that the infant is capable of producing (Jaffe, Stern, and Perry 1973). These back-and-forth interchanges may establish the basis for the later development of turn-taking in linguistic conversation.

In addition to learning turn-taking rules, children may be helped to make the transition from the attentional structures with which they come equipped (e.g., figure vs. ground) to the linguistic structures that develop later by early communicative experiences (Bruner 1974). Mothers focus infant attention on self or object in joint attention routines. ("See the pretty ball!") Once joint attention is established, mothers act on or encourage the child to act on the object, usually forming joint action rituals that are repeated over and over in play during the child's early months. ("Here, you take the ball. Good! Now give it back. Give Mama the ball. Good girl! Thank you!") As mothers remark on these ritual, predictable actions, the basic topic/comment structure of human language is repeatedly demonstrated for the child. As the child participates in the routine through attention, action, and vocalization, progress is made in the ability to distinguish agent from action and from recipient of action—distinctions that will provide the basis for semantic categories and grammatical order relationships. Although it is not clear how much interaction of this kind is necessary for language learning (Snow 1981), early reciprocal routines do appear to provide mothers with an ideal opportunity for embedding the child's actions in a meaningful social context. From this reliable data, the child can form hypotheses about the connections between words and things that can be tested in subsequent interactions. In this way, the child begins the transition from prelinguistic to conventional communication.

Early Communicative Intents. Although children's first words do not generally appear until the beginning of their second year, infants show evidence of initiating communication between 9 and 12 months of age. These nonverbal communications have been found in a variety of studies (Halliday 1975; Bates 1976; Bates et al. 1979) to express the same range of intentions. They are generally limited to requesting objects or actions, rejecting offered objects or activities, and calling attention to objects or commenting on their appearance. These intents are expressed first with nonconventional gestures, such as reaching (for requests) and pushing away (for rejection). Somewhat later, vocalization accompanies the gesture or replaces it, although the range of intentions expressed remains similar until 16–18 months of age. These vocalizations often contain intonation contours similar to those used by the adults in the child's life (Menn 1978).

Another achievement of this 9- to 12-month period is the beginning of the understanding of words. A few words associated with routine games, such as "pat-a-cake" and naming rituals will be recognized by children who have been playing these games more or less as passive responders up to this point (Bruner 1975). Now merely saying the words ("Let's play pat-a-cake!" or "Show me your nose!") in a familiar context will elicit a spontaneous action from the child (clapping, putting a hand on the nose). Comprehension is limited to these routines, however.

First Words. Conventional use of language begins around 12 months of age, when children usually say their first recognizable words. Around this time, children also show the first evidence of true lexical comprehension, responding appropriately to words outside the context of routine games (Huttenlocher 1974; Sachs and Truswell 1976). During the 12- to 18-month period, there is a rapid increase in both receptive and expressive vocabulary and an increase in successive one-word utterances. The words children learn in this period both name objects—usually those upon which the child acts (Mommy, cookie)—and encode relations among objects (all gone, more). Children also learn social words to be used in rituals such as greetings (hi, bye-bye) (Bloom and Lahey 1978). These first words are used to express ideas such as appearance ("There!"), disappearance ("All gone!"), or recurrence ("More"), which are related to the child's developing notions of object permanence (Bloom 1973). They generally serve communicative purposes similar to those achieved by the earlier gestures and vocalizations (Halliday 1975).

Toward the middle of the second year, vocabulary size reaches 50 words, and children begin combining words to form two-word "telegraphic" sentences (Brown 1973). These sentences encode a limited range of meanings, such as possession ("Daddy shoe"), location ("sit chair"), and elaboration of earlier expressions of existence ("There doggy"), nonexistence ("No milk"), disappearance ("All gone cookie"), and recurrence ("More candy") (Bloom 1970).

Linguistic comprehension in this period is not far ahead of expressive abilities (Bloom 1974). But children in their second year often appear to understand everything their parents say. They achieve this deception by employing a variety of nonlinguistic strategies that allow them to seem to be responding to what parents say, when, in fact, they are responding to what parents do or what they know to be the way things usually happen (Chapman 1978). These strategies include looking at what Mother looks at (resulting in the appearance of understanding object names, e.g., "See the ball?"), doing what is usually done (resulting in the appearance of understanding instructions, e.g., "Brush your hair"), and interpreting sentences as requests for the child to act (resulting in the apparent understanding of complex indirect requests: "Why don't you go close the door for me?").

The period from 18 to 24 months is also the time of important changes in conversational ability. Now children begin to recognize the conversational obligation to respond to speech with speech (Chapman 1981). Children reliably answer routine questions ("Where's the 'X'? What's this? What does the 'X' say?") and acknowledge their partner's comment with their own remark. Youngsters also begin to request information at this time, at first usually by asking for the names of objects. This heuristic use of language marks the beginning of the child's capacity to use words to learn about the world (Halliday 1975).

The Acquisition of Linguistic Structures. The preschool period (from 2 to 5 years) is the time in which the child's language evolves from primitive telegraphic utterances to fully grammatical forms. In addition to rapidly acquiring vocabulary—an average of 8 to 11 new words per day—the child also goes through a process of approximating more and more closely the syntax of the language spoken in the home. There is evidence of the child's active role as a syntactic hypothesis-generator in the frequent occurrence of overgeneralized forms, such as "goed," "comed," and "foots" (Cazden 1968). In these overextensions of the inflectional rules that the child has abstracted from the ambient language, forms are expressed which the child could never have heard. It is clear that children are not making these mistakes by imitating. They are producing novel—albeit wrong—forms by applying generative rules to words that happen to be exceptions to them.

As the child's grammar becomes more complex, average sentence length increases (Loban 1976; Miller and Chapman 1981). Although rates of increase vary quite widely, children tend to acquire the same syntactic structures when their sentences are approximately the same length (Brown 1973). Mean length of utterance (MLU), then, can be calculated from a sample of spontaneous speech and used to make a reliable prediction of the syntactic rules the normal child will have mastered. As structures in simple sentences approach the adult model, complex sentences using embedded ("Whoever wins can go first") and conjoined ("Then it broke and we didn't have it any more") clauses emerge (Limber 1973; Paul, Chapman, and Wanska 1980). The abilities to encode ideas syntactically ("Daddy's shoe" vs. "Daddy shoe") and to relate ideas within one utterance ("I'll fix it if you give me a bite of your candy") free the child's language from dependence on the nonlinguistic context for interpretation. While an adult had to use knowledge of the child and the situation to interpret "Daddy shoe" (The shoe that's Daddy's? Daddy put on the shoe?), the syntactically marked "Daddy's shoe" is unambiguous and interpretable by anyone.

In addition to changing in syntactic form, children between ages 3 and 5 years also change the ideas that they express in their sentences. While earlier utterances generally described actions and objects that were immediately present, sentence content expands during the preschool years to allow for reference to events remote in time and space (Bloom and

Lahey 1978). The uses to which children put their language also become more diverse (Dore 1978; Tough 1977) to include imaginative, interpretive, and projective functions. In addition, a variety of conversational skills emerge and become refined. Children increase their ability to maintain and add new information to their interlocutor's topic (Bloom, Rocissano, and Hood 1976), to clarify and request clarification of misunderstood utterances (Gallagher 1975), to make their requests politely and indirectly (James 1975; Bates 1976), and to choose the appropriate speech style on the basis of the speaker's role (Sachs and Devin 1973) and the listener's status (Shatz and Gelman 1973).

Increasing comprehension skill is reflected in the expanding number of elements that can be processed in a simple sentence (Chapman 1978). In addition, strategies for comprehending sentences change from relying on knowledge of the way things usually happen (which could lead children to interpret "The dog is patted by the mother" correctly) to reliance on linguistic rules, such as word order (which would lead them to misinterpret "The dog is patted by the mother" by assigning the first noun to be the "doer" as it would be in a simple active sentence, i.e., "The dog pats the mother") (Bever 1970; Strohner and Nelson 1974; Maratsos 1974).

The Elaboration of Language. Although children have acquired most of the sentence structure of their language by age 5 (Menyuk 1963; Tough 1977), syntactic development continues into the school years as children learn devices for elaborating their utterances (Hass and Wepman 1974) and for condensing more information into sentences by increasing the proportion of dependent clauses in narratives (Loban 1976). Children also gradually learn to use and comprehend the more complex, optional sentence types in their language, such as passives ("The boy was hit by the car") (Baldie 1976; Lempert 1978), and sentence types that violate usual rules for assigning subjects to embedded clauses ("John is easy to see" vs. "John is eager to see") (Chomsky 1969). In addition, they learn to use syntactic cues not only to decode semantic relations within sentences but also to identify the connections between sentence elements and those given previously in the discourse (Paul 1981).

Semantic and conversational abilities also continue to develop during the school years. Vocabulary size is still increasing and new words are now being learned from reading, as well as from conversation. Interestingly, the nature of children's word associations changes around age 7 from syntagmatic (association to words similar in meaning but not in grammatical class) to paradigmatic (association between words of the same class—a noun for a noun, an adjective for an adjective) (Brown and Berko 1960; Ervin 1961). These shifts in association suggest that the school-aged child's "mental dictionary" is being reorganized according to linguistic rather than episodic, or event-based, connections (Nelson 1977; Petrey 1977). School-aged children also gradually acquire the ability to communicate with precision and to take the listener's viewpoint into account in formulating an utterance (Asher 1978).

A final aspect of language that undergoes important developments in the school years is metalinguistic awareness, the ability to use language to talk about language and to examine language apart from the objects and events to which it refers. Children recognize the difference between words and their referents around age 6 (Pease 1981). They use their metalinguistic skills to create words (Clark 1980) and to develop codes and secret languages (Ferguson and Macken 1980), probably in the service of increasing social solidarity among peers during the preteen and teenage periods. Metalinguistic awareness is also important in the development of reading and writing abilities (Mattingly 1972).

Changes in the Focus of Child Language Research

Since the early 1960s, the study of language acquisition has undergone a series of shifts in direction. Chapman (in press) identifies five major shifts that have had important consequences for the study of language disorders. The first involved a change in theoretical models of the motivating force behind developmental progression. While transformational grammar implied that syntactic acquisition proceeds relatively autonomously as a result of the unfolding of innate grammatical capacities, investigators in the early 1970s were forced by their data to examine the semantic limitations they discovered in early speech in terms of developing cognitive abilities (Sinclair 1970, 1971, 1973; Bloom 1971; Slobin 1973; Beilin 1975; Cromer 1976). In the latter half of the decade, it became clear that simple cognitive prerequisites for specific linguistic skills were not easy to find (Miller et al. 1980). Attention then shifted to the role of social-communicative skills as the guiding force behind language development (Bates 1976; Bates and MacWhinney 1979; Greenfield 1979; Greenfield and Dent 1979). As a result, interest in pragmatic achievements such as the emergence of communicative intention, turn-taking, topic maintenance, and speech style adjustments to particular social situations became (and continue to be) a major focus of research (for a review, see Rees 1978).

A second shift involved a move away from comparing child language to adult rules. In recent years, attempts have been made to examine primitive utterances not as "mistakes," but as the output of a set of rules that are different from those used by adults to generate sentences. The task has been to describe these child-specific rules and to identify their contexts and scope of application.

Although these child language rules appear to be used with remarkable uniformity (Klima and Bellugi 1966; Brown 1973), there are certainly individual differences in language acquisition. These are now becoming the object of examination (Nelson 1973, 1981; Bowerman 1973). An attempt is being made to understand the diversity of patterns and styles available for normal acquisition and the effects of cultural differences on language learning (Blount 1970; Mitchell-Kernan 1971). A related change in the focus of this research is a shift from the study of macrodevelopment—the broad outlines of acquisition—to microdevelopment—the detailed histories of the evolution of single rules (Bloom, Miller, and Hood 1975; Menn 1978; Bates et al. 1979). These studies have illuminated the early limitations of linguistic rules and underline the gradual, sometimes effortful process of increasing generalization and the amount of active learning necessary to expand the contexts in which rules can apply.

A final shift that is relevant to work in language disorders was the change from accepting speech (production or expressive language) as the single index of language development to the realization of the importance of investigating language comprehension (Bloom 1974; Ingram 1974; Chapman and Miller 1975, 1980). This shift led to analyses of the relations between the two modes of language and the recognition that the simple notion that "comprehension precedes production" cannot account for many aspects of the child's performance. This discovery has resulted in the building of new and more complex theoretical models of linguistic processing in the language-learning child (Bloom and Lahey 1978).

These changes in thinking about language development have had profound effects on the understanding of childhood language disorders. For example, the shift in emphasis from syntax, alone, to the meaning (semantic) and contextual (pragmatic) aspects of language has allowed clinicians to identify and describe pervasive deficits in communicative competence and to look at the conceptual and social abilities that may be basic to the failure to acquire language. As another example, examining the child's own rules, rather than identifying mistakes, allows investigators to compare children who suffer from developmental disorders, not to adults, but to their normal peers and to decide whether their language is delayed (similar to that of a younger, normal child) or deviant (showing an atypical system of intermediary rules). A review of current conceptions of communication disorders will reveal the extent to which they have benefited from the dialogue with research in normal development.

Current Views of Developmental Disorders of Communication

The model of language acquisition presented here implies that the development of communicative competence is not a strictly linguistic achievement. Rather, it is the result of the complex coordination of a set of interacting systems including those involved in perceptual, cognitive, and social functioning, to name but a few. The model predicts that breakdown at any point in this finely tuned orchestration will result in impaired language ability. Certain of these impairments can be traced easily to malfunctions in one of the systems subserving language development. Communication problems associated with congenital hearing impairment constitute an example. Here, failure to talk and understand speech is simply a result of lack of access to the auditory signals that contain linguistic information. Other failures to learn language are less easily traced to specific causes. Mentally retarded youngsters, for example, will usually acquire language commensurate with their mental age. Yet, in some cases, these children have language deficits that exceed their cognitive limitations. These deficits may encompass not only linguistic structures but more basic failures of communicative intention. Other children without any apparent sensory or intellectual dysfunction nonetheless fail to learn to talk, or learn exceedingly slowly. In these youngsters, too, social-communicative deficits may accompany the linguistic disorder. The severity of these disabilities can vary from total absence of both language and communicative function to slight delays relative to the child's overall mental age. Idiosyncratic or deviant structures may also be present.

Two main categories can be identified within this more puzzling class of language disorders: childhood aphasia and primary autism. Although the two have similar features, there are several characteristics that distinguish between them (Cohen, Caparulo, and Shaywitz 1976; Fay and Schuler 1980). Children who can be labeled "aphasic" generally seem perfectly normal, healthy, and social during their first 2 years of life. Parents become anxious about them only when, by the end of the second or during the third year of life, they are not talking or are talking very little. Many of these children create their own gestural system for augmenting their limited linguistic communication skills, and some benefit from instruction in Total Communication using American Sign Language. Although they may become frustrated and disturbed about their communication difficulties and may develop behavioral problems as they become older, they do establish meaningful social relationships and have a consistent history of doing so. In addition, they generally can engage in purposeful play with objects and show evidence of the ability to imagine and pretend.

On the other hand, those children categorized as autistic not only fail to talk during the preschool period, they also have a long history of poor or nonexistent social relationships—even with their often devoted parents. They show poor motor imitation skills, their play with objects is disorganized, and personal gesture systems rarely serve any communicative function. When autistic children do develop language, it has peculiar characteristics, such as pronoun reversals, protracted echolalia, the use of words for highly personalized meanings, and a deliberate, stiff quality of speech with unusual intonation contours. Although aphasic children often develop distractibility, aggressiveness, and social withdrawal that may make them appear autistic-like as they become older, their language will generally sound like that of a younger, normal child and will not display these peculiarities.

There may, of course, be mixed syndromes of these disorders, and children may experience multiple handicaps, such as a coincidence of hearing impairment and developmental aphasia. In an interactive model of language development such as the one presented here, any component or components of the system can malfunction, and these malfunctions will result in language disorders that vary in their features depending upon the underlying capacities that are disturbed. Despite this possibility, developmental aphasia and primary autism do exist as distinct clinical entities that can be identified in their "pure" form in some children and recognized as components of a disorder in others. The present model would postulate that each of these syndromes arises from specific dysfunctions in one of the developing systems that contribute to intact language use, even though the precise nature of the dysfunction has not yet been identified. Such a model, derived from the interactive conception of language development that has arisen from recent research, allows the entire spectrum of language disorders to be placed in an integrated framework.

In addition to providing an inclusive structure for viewing the disorders of language learning, the shift in language acquisition studies away from syntax, alone, toward broader aspects of communicative competence makes communication assessment possible even in children who are not talking. Measures of nonverbal communicative function drawn from observations of preverbal communication in normal infants can now be applied to analyzing the interactions of children without overt language. In this way, more precise diagnoses can be made at an early point in the child's development. (See Appendix for a sample interview for assessing the history of development of prelinguistic communication skills.)

The current emphasis of research on normal children is on discovering the child's own rule system; that emphasis has also provided insights into disordered children's behavior. One example is Fay's (1969, 1973; see, also, Fay and Schuler 1980) analysis of echolalia in autism. Instead of assuming that echolalia is a "mistake" in the use of language, Fay explores the purpose it serves for the child. He concludes that echoing gives the linguistically incompetent youngster *something* to say in order to continue a conversation. Echolalia appears, then, to serve an important phatic function for the autistic child—it keeps the lines of communication open and prolongs interaction. This analysis has important implications for the treatment of echolalia in the therapeutic setting. Understanding its function will make clinicians more wary of attempting to extinguish echolalia before more effective means of maintaining interaction have been substituted for it.

Psycholinguistic interest in the range of individual differences along the spectrum of normal development has contributed to clinical ability to assess language disorders. Having a quantitative notion of the normal range allows the clinician to make more reliable decisions about when a problem, in fact, exists. Miller and Chapman's (1981) studies of normal variation in mean length of utterance, for example, provide an index of language delay that can be of great value in deciding when children are so far behind agemates that intervention is required. There is now a reliable way of deciding when too long a time has elapsed for children to "grow out of" their failure to use words. The orientation in acquisition research toward microscopic analysis of development also has clinical applications. Looking at the development of single rules—from their early, limited sphere to their eventual generalization—provides models for teaching generative rules to children who have not learned them on their own.

The shift in child language research from production to comprehension has especially great significance for clinical work. Language disorders have traditionally been evaluated only in terms of productive deficits; little attention has been paid to the relation between expression and understanding. But it may be the case that some children who have been called "aphasic" suffer only from minor lags in receptive ability. In that case, *aphasia*, with its connotation of deficits in symbolic ability, may be a misnomer. For some of these children, failure to speak may be a result of more circumscribed neuromotor disabilities. This diagnosis would, of course, have important implications for treatment. An increasing awareness of the importance of evaluating speech and understanding independently will help in making such distinctions in the future.

Directions in the Study of Language Disorders

Research in communication development has contributed in many ways to the study of language disorders. At the same time, information from investigations of language disorders is valuable in deepening the understanding of, not only the disorders themselves, but the nature of language and its acquisition. What are the questions about disordered language, the answers to which would serve this dual purpose? One question is the relationship between language and cognitive development in language disorders, such as childhood aphasia and primary autism. Older aphasics, for example, fail to develop abstract thought and vocabulary (Caparulo and Cohen 1977), and there is a need to look more closely at the relations between language and thought in these youngsters. What specific subskills in the sequence of cognitive development might show deficits that would predict and contribute to language disturbance? What effects do limited linguistic skill have upon the development of high-level cognitive organization, which ordinarily relies so heavily on language as a mediating device? Will children with severe language disorders eventually develop deficits in problem-solving ability and disorders of thought as a result of their inability to represent and organize experience in language? The answers to these questions will contribute not only to diagnostic and prognostic capacity, but also to the understanding of the relations between language and thinking in normal individuals.

Similarly, more careful analysis of connections between social and linguistic performance in children with disorders will improve diagnostic and prognostic power, as well as shed light on the social bases of normal language acquisition. The area of mother-child interaction is particularly fertile ground for investigating this question, especially in light of the wealth of information now available on typical mother-child communication. What very early mismatches that appear in the mother-infant dialogue will predict later language-learning problems? How do parents react to absent or disorganized social behavior? Is there a response that optimizes the child's chance for progress? (See Cohen, Caparulo, and Wetstone, in press, for an initial approach to this question.) This information would lead to a better understanding of the aspects of mother-child interaction that are necessary for language development, in addition to providing categories for early assessment.

The suggestion that disorders of perceptual and attentional regulation are also present in aphasic and autistic children represents another piece of the puzzle to be assembled in understanding these disorders (Caparulo and Cohen 1977). Although it is clear from the infant studies cited above that perception and attention are highly organized even in newborns, the relations among perception, attention, and communication are not yet clear. Simple prerequisite relations will probably fail to explain clinical observations that identify attentional deficits developed after the language-learning period in aphasic youngsters (Cohen, Caparulo, and Shaywitz 1976).

The relations between social and cognitive development are also of interest in building models of the interweaving of skill components in language. For example, is the observation of Bates et al. (1979) that language use correlates highly with performance on means-ends tasks (Uzgiris and Hunt 1975) true for this population? Might some language disorders be the result of, not a global, but a rather limited cognitive failure, perhaps a failure to understand relations between means and ends? Could this failure, in turn, lead to a deficit in social understanding, i.e., that people can serve as a means to desired ends if the tools for manipulating them (communication) are used?

Finally, the relations between the modes of language in these populations merit further investigation. What is the typical relationship between speaking and understanding in children with language disorders? Can subgroups within populations be isolated on the basis of receptive/expressive distinctions? Certainly, children who fail to develop receptive abilities will be impaired in their expressive language as well. But might the opposite relationship be true? Could the inability to talk also impede progress toward the ability to decode complex linguistic signals?

All of these questions center around one fundamental issue in the study of normal communication and its disorders: How do the components of the communication system interact in development? Which components are necessary, sufficient, or simply associated with the growth of which others? Are the more puzzling disorders of language learning actually the result, not of global, but of highly specific, underlying failures of social-cognitive function? Or, on the other hand, do they, in some cases, cause disorders of thinking and relating because of the inability to use language to mediate thought and interaction? Not only will study of the language of communicatively impaired children improve therapeutic intervention, it will also contribute to understanding the complex integration of abilities that results in the normal child's remarkable achievement in mastering a first language.

Appendix. An outline for a communication development interview

Age	Communication developmental milestone	Question for parents	Reference
0–2 months	Responsiveness to sounds in the speech frequency range	Does the child turn head or look up at the sound of voices?	Hutt et al. (1968)
	Preference for speech over other rhythmic sounds	Can the child be soothed or made to smile by the sound of voices? Does the child seem to like listening to people talk?	Butterfield and Siperstein (1974)
	Tendency to synchronize movements to breaks in speech	Does the child seem aware of when you stopped talking? Does the child wait for a pause to reach or move?	Condon and Sander (1974)

Appendix. An outline for a communication development interview—*Continued*

Age	Communication developmental milestone	Question for parents	Reference
	Categorical perception for speech sounds		Eimas et al. (1971)
	Preference for human faces over other visual stimuli	Does the child attend to your face? Does the child seem to look at you more often than at other things when you are in the room?	Fantz (1961, 1963, 1966); Kagan and Lewis (1965)
2–8 months	Mother-child "dialogue" in mutual gaze, joint action, babbling	Does the child "talk back" to you when you talk "baby talk"? Can you direct the child's attention to objects? Does the child seem to enjoy playing with you using toys, playing games such as "pat-a-cake" or "So big"?	Jaffe, Stern, and Perry (1973); Bruner (1974)
9–12 months	Expression of nonverbal communicative intents to request, reject, call attention to self and object	Does the child make wants and needs known by gesturing and making sounds? Does the child attempt to get your attention this way? Does the child attempt to get you to play games or comment on his or her activities?	Halliday (1975); Bates (1976)
	Understanding a few words in routine contexts	Does the child eventually recognize a few words from games such as peek-a-boo and act spontaneously when he or she hears the word?	Bruner (1975)
12–18 months	Use of first recognizable word	Does the child use any words to express wants and needs?	Bloom (1973)
	Understanding of words outside routine contexts	Does the child understand any words without gesture or facial cues? For example, if you said, "Where's Daddy?" would the child turn and look for him?	Huttenlocker (1974)
18–24 months	Two words combined to form telegraphic sentences expressing a limited range of meanings	Does the child put words together in two-word sentences?	Bloom (1970); Brown (1973)
	Understanding of words for absent objects	If you ask for an object in another room, can the child fetch the correct item without gestural clues?	Miller et al. (1980)
	Understanding of conversational obligation to respond to speech with speech	Does the child attempt to answer questions or respond to your comments in some way, verbal or nonverbal?	Chapman (1981*a*)
	Use of language to request information	Does the child ever either verbally or nonverbally try to get you to say the names of objects?	Halliday (1975)

Appendix. An outline for a communication development interview—*Continued*

Age	Communication developmental milestone	Question for parents	Reference
2–5 years	Average sentence length increases from 2.0 to 4.5 words or more	Does the child gradually add more words to sentences?	Loban (1976); Miller and Chapman (1981)
	Rules for forming plurals, past tense, etc., are overgeneralized	Does the child ever say words wrong, such as *comed, goed,* or *foots*?	Cazden (1968)
	Mastery of morphological and syntactic rules for simple sentences; emergence of complex sentences	Do the child's sentences eventually sound more like an adult's?	Klima and Bellugi (1966); Brown (1973); Limber (1973)
	Use of linguistic rules for understanding sentences	Does the child ever misunderstand things you say, especially when you use long or complicated sentences?	Bever (1970); Maratosos (1974); Strohner and Nelson (1974)
	Use of language to talk about events remote in time and space	Does the child tell you about things that happened away from home? In the past?	Bloom and Lahey (1978)
	Use of language for diverse purposes, such as imagining, predicting, interpreting	Does the child talk about things that will happen later? Could happen? Does the child talk about "make-believe" things?	Tough (1977)
	Increased conversational skills; topic maintenance	Can the child stick to a subject in conversation, say something new about the subject?	Bloom, Rocissano, and Hood (1976)
	Clarification	If the child doesn't understand you, does he or she ask you to repeat? Can the child repeat or repair a sentence you misunderstand?	Gallagher (1975)
	Polite, indirect requests	Can the child use language to "wheedle something out of you"? Can the child "say it nicer" in other ways than just adding *please*?	James (1975); Bates (1976)
	Choice of the appropriate speech style for the social situation	Does the child talk differently to younger children? Is the child more polite to grownups than peers?	Sachs and Devin (1973); Shatz and Gelman (1973)
5–12 years	Use of devices to elaborate and condense information in sentences	Can the child tell stories without stringing sentences together only with *and*?	Hass and Wepman (1974); Loban (1976)
	Ability to use and understand unusual sentence types in the language, such as *passives*	Does the child sometimes use complex sentence forms in speaking? Writing?	Chomsky (1969); Baldie (1976); Lempert (1978)

Appendix. An outline for a communication development interview—*Continued*

Age	Communication developmental milestone	Question for parents	Reference
	Development of metalinguistic awareness	Does the child ever make up words, play games with words, make up puns? Could the child tell you his or her favorite word?	Mattingly (1972); Pease (1981)

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Thyroid Function in Developmental Disorders

by J. Gerald Young and Donald J. Cohen

Abstract

The relationships between catecholamines and thyroid state are considered from clinical and molecular perspectives. The effects of thyroid hormone on adrenergic systems are mediated by altered receptor and postreceptor function. Clinical symptoms of major childhood neuropsychiatric disorders, as well as related biological measures, may be influenced by thyroid hormone regulation.

Interactions between the thyroid and catecholamine systems are clinically evident in the close resemblance of symptomatology of the hyperthyroid state to β-adrenergic effects (tachycardia, increased systolic blood pressure, increased myocardial contractility, and tremor are common) (DeGroot and Stanbury 1975) and the clinical response of hyperthyroid patients to β-adrenergic antagonists (e.g., propranolol) (Mazzaferri et al. 1976; *Lancet* editorial 1980). On the other hand, newly admitted psychiatric patients may have transient thyroid dysfunction in which hyperthyroidism is associated with mania, severe anxiety, agitation, and thought disorder, while hypothyroidism is related to alcohol, hypnotic substance abuse, and weight gain (Kolakowska and Swigar 1977; Cohen and Swigar 1979; Swigar et al. 1982).

Experimental observations at the molecular level give further evidence of a thyroid-catecholamine interaction (e.g., the negative relation between thyroid function and indices of catecholamine function, such as catecholamines and their metabolites and related enzymes) (Ho-Van-Hap, Babineau, and Berlinguet 1967; Klawans and Shenker 1972; Christensen 1973; Stoffer et al. 1973; Cohen et al. 1974; Nishizawa et al. 1974; Noth and Spaulding 1974). Nevertheless, several factors complicate the interpretation of these data. First, the relations described at the clinical and molecular levels differ. At the organ or systemic level, as manifest in observable symptoms, the catecholamine and thyroid effects act in the same direction, that is, a component of hypothyroidism is a hypoadrenergic state. On the other hand, at the molecular level, the data document an inverse relation in which abnormally high thyroid hormone levels are accompanied by indices suggesting reduced catecholamine function. This apparent contradiction is theoretically resolved by hypothesizing changes in receptor state, ultimately leading to congruent effects at cellular and systemic levels.

Second, relations between the thyroid and catecholamine systems differ across species and in different tissues of the same species (Tong and D'Iorio 1976; Ho-Van-Hap, Babineau, and Berlinguet 1967). Generalizations from one tissue to another are precarious; this is especially important in clinical studies in which lack of access to brain tissue requires indirect measures of catecholamine function to infer similar effects in brain.

Third, a clear negative relation between thyroid function and indices of catecholamine function

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may be evident for some indices only when thyroid function is outside the normal range. Inclusion of subjects with normal thyroid function may obscure an otherwise observable relation.

Fourth, thyroid functional effects at the cellular level are consequent to the action of at least two hormones, triiodothyronine (T_3) and thyroxine (T_4) (Sterling 1979*a*, 1979*b*). In addition, a substantial portion of T_3 active at cellular sites is derived from peripheral conversion of T_4. Use of a single measure (such as serum T_4) to indicate metabolic effects of the thyroid must be cautious (Ingbar and Braverman 1975).

Strong evidence for thyroid hormone effects on receptor function comes from several sources. Electrophysiological studies at the neuronal level have indicated postsynaptic changes in altered thyroid states. For example, Purkinje cells of the rat cerebellum, the discharge rate of which is largely determined by tonic inhibitory noradrenergic afferents from the locus ceruleus, fire at a faster rate in hypothyroid rats; Purkinje cells are also less sensitive to iontophoretically applied norepinephrine. The subsensitivity of the Purkinje cells to norepinephrine is reversed by administration of T_3 (Marwaha and Prasad 1981).

Second, binding studies of adrenergic receptors have demonstrated a decrease in the number of β-receptors in hypothyroid states (Banerjee and Kung 1977; Ciaraldi and Marinetti 1977; Williams et al. 1977; Hoffman and Lefkowitz 1980; Bilezikian and Loeb 1982), which fits well with the subsensitive response of the cell to norepinephrine in the hypothyroid animal. Third, diminished adenylate cyclase activity in peripheral tissues has been observed in hypothyroidism (Levey, Skelton, and Epstein 1969). Thus, the sum of the evidence to date converges to indicate thyroid modulation of cellular response to noradrenergic neurotransmission by enhancing postsynaptic receptor response and increasing overall noradrenergic effects at organ and systemic levels (Whybrow and Prange 1981).

There is another viewpoint from which thyroid-catecholamine interactions are critically important to researchers. Given the strong evidence of these interactions, thyroid function stands as an important source of variance to be considered in studies of catecholamine metabolism. The nature of the thyroid-catecholamine interactions must be specified, so that there is less likelihood that they will act as confounding factors in experimental procedures not targeted on thyroid effects.

The implication of thyroid effects as contributors to the regulation of activity level and sympathetic function, each an important focus of research in major neuropsychiatric disorders of childhood, led to research designed to clarify thyroid actions in these disorders (Cohen et al. 1974, 1980; Young et al. 1982*b*). In a series of studies of normal subjects and patients with psychiatric or endocrine disorders (Young et al. 1982*a*, 1982*c*; Young, Kyprie, and Cohen 1982) described in this issue of the *Schizophrenia Bulletin*, the interaction between thyroid regulation and catecholamine-related enzymes was investigated. These studies exemplify approaches to dissecting the relation between the neuroendocrine system and neuronal function in clinical research.

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Catecholamine-Thyroid Hormone Interactions: I. Thyroid Hormone and Platelet MAO Activity in Psychiatrically Disturbed Children

by *J. Gerald Young, Reza Feiz, Jerome A. Roth, Merilyne C. Waldo, and Donald J. Cohen*

Abstract

The relation between platelet monoamine oxidase (MAO) activity and serum thyroxine indices was investigated in 68 children and adolescents with a psychiatric disorder and 45 healthy controls. Thyroxine indices were similar in patients and control subjects and neither thyroxine nor estimated free thyroxine levels were significantly related to platelet MAO activity.

Thyroid hormones are intimately related to mood and behavior, as is vividly evident in the anxiety and agitation of hyperthyroidism and the lethargy of the hypothyroid state. Extremes of activity (augmented or reduced) seen in severe developmental disturbances are often target symptoms for medication, and triidothyronine (T_3) has been used in the treatment of childhood psychoses with a beneficial effect in some children (Sherwin, Flack, and Stokes 1958; Campbell et al. 1972). The basis for this therapeutic effect is unknown, but the interaction of thyroid hormones with catecholamines or indoleamines might play a role.

Subgroups of autistic children have been characterized by elevated whole blood serotonin (Schain and Freedman 1961) and decreased urinary free catecholamines (Young et al. 1978). Serotonin and the catecholamines are degraded by the intraneuronal enzyme monoamine oxidase (MAO). MAO activity has been reported to have a negative relation with thyroid hormone levels in some animal and human tissues (Skillen, Thienes, and Strain 1961; Levine et al. 1962; Ho-Van-Hap, Babineau, and Berlinguet 1967; Tong and D'Iorio 1976; Feldman and Roche 1977), although not all, and may have a significant regulatory function in nerve endings. In order to clarify whether thyroid function is a source of variance in platelet MAO activity, and to better understand the basis for a therapeutic effect of T_3 in some disturbed children, we studied the relation between platelet MAO activity and thyroid indices in children with psychiatric disturbances and a control population.

Population and Method

The subjects of this study were 68 children and adolescents with a psychiatric disorder and 45 healthy controls. The mean age of the 113 subjects was 17.2 years; the patients were younger than the control subjects in both the male (11.9 vs. 27.8 years) and female (12.1 vs. 21.9 years) groups. Each child received a detailed medical and psychiatric evaluation. The severity of disturbance in the patient group ranged from moderate to extreme. All subjects were in good general health at the time of this study. Twenty-eight percent were taking medication, usually psychotropic drugs, anticonvulsants, or multivitamins. Normal control subjects had no history of medical or psychiatric disturbance either personally or in their families; family control subjects had no medical or psychiatric illness, but were related to a child with a developmental disturbance.

Blood was obtained by standard venipuncture, and collected in

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glass tubes containing 10.5 mg EDTA (K_3) which were immediately placed on ice. Within 3 hours of collection, platelets were separated by centrifugation and stored frozen for a maximum of 14 days before assay. ^{14}C-Tyramine was used as substrate and platelet MAO activity was expressed as nmoles deaminated product formed per mg protein per 60 minutes of incubation. (Roth, Young, and Cohen 1976).

Thyroxine indices were determined using a competitive protein binding technique (Seligson and Seligson 1972, 1978). Thyroxine (T_4, μg/100 ml) and residual thyroxine binding capacity (TBC, μg/100 ml) were measured and the following derived values were obtained: total thyroxine binding capacity (TTBC, μg/100 ml), percent thyroxine saturation of TTBC (% TS), and estimated free thyroxine (EFT, ng/100 ml).

Results

There were no differences in any of the thyroxine indices among the control and patient groups and all were in the normal range. Male patients had a higher platelet MAO activity than male control subjects, as described elsewhere (Young et al. 1980).

No simple relation emerged when the correlation coefficients for MAO activity and the measured or derived T_4 indices were examined (table 1). There was a trend toward a negative association between MAO activity and thyroxine in the female group, but neither T_4 nor EFT was related to MAO activity in males. There was a significant negative association between MAO and TBC of moderate strength among the females and male controls; this relation did not hold in the overall male population or the male patients. The same relations were examined using third order partial correlations (controlling for age, platelet count, and hematocrit); there was no substantial change from the values given in table 1.

Discussion

Norepinephrine turnover in the rat heart increases following hypophysectomy or thyroidectomy, but returns to normal with thyroid replacement therapy (Landsberg and Axelrod 1968). Plasma norepinephrine (NE) (Christensen 1973; Stoffer et al. 1973), plasma dopamine-β-hydroxylase (DBH) (Noth and Spaulding 1974), and spinal fluid homovanillic acid (HVA) (Klawans and Shenker 1972), the principal brain metabolite of dopamine, are increased in hypothyroidism and decreased in thyrotoxicosis. This negative relation between thyroid state and catecholamine levels has been hypothesized to result from altered β-adrenergic receptor number (Williams et al. 1977; Sterling 1979), or transformation of iodothyronines (tyrosine analogues) into adrenergic neurotransmitters (Dratman 1974; Dratman et al. 1976).

The negative association between thyroid activity and MAO activity in some tissues suggested that MAO might play a part in this regulatory cycle, or might be affected by thyroid function. This would be important to understand for metabolic studies and treatment of severely disturbed children, as well as for elucidating a possible source of variance in studies of platelet MAO activity.

In this study, EFT, the measure of active thyroid hormone in the blood, bore no relation to platelet MAO activity. However, there was

Table 1. Platelet MAO activity and T_4 indices in children with psychiatric disturbances and controls: Pearson correlation coefficients

Variables	Normal controls	Family controls	All controls	Patients	Total population
Males					
Number	15	10	25	50	75
MAO—T_4	−.36	−.02	−.18	.12	.08
MAO—TBC	−.24	−.68**	−.41**	.15	−.02
MAO—EFT	−.06	.39	.18	.01	.08
Females					
Number	11	9	20	18	38
MAO—T_4	−.68**	−.43	−.51**	−.27	−.41*
MAO—TBC	−.74***	−.72**	−.71****	−.40	−.62***
MAO—EFT	.12	.49	.32	.12	.28*

*$p < .10$.
**$p < .05$.
***$p < .01$.
****$p < .001$.

a negative association between total T_4 level and MAO activity in females. A moderately strong negative association between residual T_4 binding capacity (TBC) and platelet MAO activity in females and in male controls was notable, but its source and significance are not clear.

This association between platelet MAO activity and residual binding capacity (TBC) in women might reflect a greater total binding capacity (TTBC) secondary to the presence of estrogens and absence of testosterone; TBC tends to parallel TTBC (Robbins, Rall, and Gorden 1974).

The relation between thyroid hormone and platelet MAO activity can be considered from several vantage points. First, there are multiple molecular forms of MAO. The structural basis for these different forms is not yet clear; currently MAO is divided into Type A or Type B according to substrate and inhibitor characteristics (Fowler et al. 1978). The various responses of MAO in different tissues to thyroid hormones may reflect its multiple forms. Second, when T_4 and T_3 are compared, T_3 has been shown to be less firmly bound to protein, to have a shorter biological half-life, and to have a biological activity some four times greater than that of T_4. If T_3 is, in fact, the physiologically active hormone, then it might be useful to measure T_3, rather than T_4. However, most of the T_3 is derived from the peripheral deiodination of T_4, and if the higher concentration of both free and bound T_4 in the plasma is considered together with its longer half-life, the contributions of free T_4 and free T_3 appear to be comparable (Martin 1974; Ingbar and Braverman 1975). Thus, T_4 continues to be the preferred measure for thyroid hormone activity. Third, the age of the organism is crucial when considering the effect of a possible interaction between MAO and thyroid hormones. Thyroid hormones have their major impact on the brain during the critical early period in the life of the young organism. Brain tissue then has mitochondria with a functional site responsive to thyroid hormones, but this sensitivity is lost as the organism matures (Sokoloff 1977). Similarly, the effect of thyroid hormones on heart MAO in male rats changes from an augmenting one in young rats to a diminishing one in the mature animal (Ho-Van-Hap, Barbineau, and Berlinguet 1967). It appears that MAO develops at different rates in different parts of the brain and is subject to a variety of external influences which may alter the course of its development. However, other studies have provided evidence that brain MAO activity in several animals remains remarkably constant with age (Eiduson 1972; Diez and Maderdrut 1977). The subjects in this investigation were much beyond such an early period, and another study of the interaction of platelet MAO activity and thyroid hormone in pregnancy and delivery could clarify these early developmental issues.

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Catecholamine-Thyroid Hormone Interactions:
II. Thyroid Hormone and Platelet MAO Activity in Patients With Thyroid Disorders

by J. Gerald Young, Melinda M. Sprague, Donald J. Cohen, Jerome A. Roth, and Myron Genel

Abstract

Platelet monoamine oxidase (MAO) activity and serum thyroxine indices were determined in 62 children and adolescents currently undergoing medical treatment for various thyroid disorders. The platelet MAO activity of these patients was similar to that of control and contrast groups previously reported, and there were no differences when patients were grouped according to specific thyroid disorders. Estimated free thyroxine and total thyroxine levels were generally in the upper normal or slightly elevated range and were not significantly related to MAO activity.

Monoamine oxidase (MAO) is a critical enzyme in the degradation of catecholamines and serotonin, and its function at the extremes of the usual range of activity in platelets has been associated with psychiatric disorders in childhood (Young et al. 1980) and adulthood (Wyatt, Potkin, and Murphy 1979). Thyroid disease has a profound effect on the function of the nervous system (Sokoloff 1977), and thyroid hormone exerts a regulatory effect on MAO activity in several animal tissues (Skillen, Thienes, and Strain 1961; Ho-Van-Hap, Babineau, and Berlinguet 1967; Tong and D'Iorio 1976). This regulation may occur, in part, through facilitating effects of thyroid hormone on the synthesis and stability of flavoprotein enzymes such as MAO (Rivlin 1974).

The nature of the association between thyroid function and MAO activity differs according to the sex, age, tissue, species, and the substrate used when determining MAO activity (Skillen, Thienes, and Strain 1961; Ho-Van-Hap, Babineau, and Berlinguet 1967; Tong and D'Iorio 1976; Young et al. 1980). There appear to be separate thyroid hormone effects on the two isoenzymes, Type A MAO and Type B MAO (Tong and D'Iorio 1976; Cawthon and Breakefield 1979).

There have been few studies of MAO activity in human tissues during active thyroid disease. Among the relevant findings reported are the following: Adult hyperthyroid patients had increased urinary excretion of 5-hydroxyindoleacetic acid (5–HIAA), the major serotonin metabolite, with a subsequent decrease when the patients were rendered euthyroid (Skanse and Hanson 1962; Kljatschko and Stoilow 1970); hypothyroid patients had normal (Haverback, Sjoerdsma, and Terry 1956) or decreased (Kljatschko and Stoilow 1970) urinary 5–HIAA. MAO activity in jejunal mucosa from hyperthyroid patients was decreased, while jejunal MAO activity from hypothyroid patients was increased (Levine et al. 1962). While elevated serum serotonin has been reported in hyperthyroidism (Kljatschko and Stoilow 1970), another study failed to find an abnormal serum serotonin concentration in a hyperthyroid population or altered platelet MAO activity in either hyperthyroid or hypothyroid patients (Feldman and Roche 1977).

We have studied the effects of development on a series of

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biogenic amines and related compounds (Young et al., in press); both platelet MAO activity (Young et al. 1980) and estimated free thyroxine in the serum (Young et al. 1982*b*) decline in males during childhood and adolescence, suggesting that thyroid hormone might have a regulatory effect on the development of the activity of this flavoprotein enzyme. There was no clear relation between platelet MAO activity and thyroxine indices in either a population of children and adolescents with psychiatric disorders or a control group (Young et al. 1982). Both of these populations had normal thyroid function. Since an observable functional interaction between thyroid hormone and MAO activity might occur only when thyroid function is outside the normal range, we investigated the relation between thyroid hormone and platelet MAO activity in young patients with thyroid disorders who were being treated with appropriate medications. If thyroid hormone has a significant regulatory effect on platelet MAO activity, it might be most visible in states of insufficient or excessive thyroid function, secondary to either underlying disease or the pharmacological treatment employed.

Subjects and Methods

Subjects were 62 children and adolescents (19 males, 43 females) being treated in the pediatric endocrinology clinic at Yale-New Haven Hospital. They ranged in age from 3.9 years to 22.5 years. All but six were taking medication, including desiccated thyroid (15), levothyroxine (26), propylthiouracil (9), methimazole (2), and several others. Functional diagnoses were primary hypothyroidism, congenital or acquired (13); secondary hypothyroidism, with hypothalamic or pituitary dysfunction (10); hyperthyroidism (19); euthyroid thyromegaly, thyroiditis (17); and simple goiter (3). Patients with a simple goiter were grouped separately from other patients with euthyroid thyromegaly who also had thyroiditis, as indicated above. Thyroiditis was determined to be present if a patient had positive circulating antibodies, either by microsomal complement fixation or hemagglutination antithyroglobulin techniques. Platelet MAO activities and serum thyroxine indices have been reported separately for a normal control group and for children and adolescents with psychiatric disorders (Young et al. 1982*a*).

MAO activity was assayed using a previously described method (Roth, Young, and Cohen 1976) and serum thyroxine indices were determined in the Clinical Chemistry Laboratory of Yale-New Haven Hospital using a competitive protein binding technique (Seligson and Seligson 1972, 1978). Thyroxine (T_4, µg/100 ml) and residual thyroxine binding capacity (TBC, µg/100 ml) were measured and the following derived values were also reported: total thyroxine binding capacity (TTBC, µg/100 ml), percent thyroxine saturation of TTBC (%TS), and estimated free thyroxine (EFT, ng/100 ml). Normal ranges for these indices in this laboratory are as follows: T_4 = 4.6–9.2 µg/100 ml; TBC = 16.8–25.7 µg/100 ml; TTBC = 22.9–36.7 µg/100 ml; %TS = 16.0–35.0 percent; EFT = 1.0–2.1 ng/100 ml.

Results

Platelet MAO activity differs in males and females (Young et al. 1980), so results are presented separately. The mean MAO activity did not differ from activity in control and contrast groups reported elsewhere (Young et al. 1980) (tables 1 and 2). There were no significant differences in platelet MAO activity among the diagnostic groups. Free and total serum T_4 levels were generally in the upper normal or slightly elevated range in the diagnostic groups, and binding levels were not unusual (tables 1 and 2).

With one exception, there were no significant correlations between individual T_4 indices and platelet MAO activity (table 3). There was a negative correlation between MAO activity and residual T_4 binding capacity in the male primary hypothyroid group ($r = -.88$, $p < .05$). Grouping the patient population by the medication used, and assessing group means and the relation between platelet MAO activity and individual T_4 indices did not yield any significant findings.

Discussion

Altered thyroid function did not bear any consistent relation to platelet MAO activity in this group of young patients undergoing medical treatment for thyroid disorders. The corresponding correlations in female control subjects differed. In female control groups there was a negative relation between platelet MAO activity and total T_4, a moderately strong negative relation between platelet MAO activity and residual T_4 binding capacity, and a trend to-

Table 1. Thyroxine indices and platelet MAO activity of males with thyroid disorders: Means and standard deviations

Variables	Simple goiter (*n* = 0)	Hyperthyroid (*n* = 3)	Primary hypothyroid (*n* = 6)	Euthyroid thyromegaly, thyroiditis (*n* = 2)	Secondary hypothyroid (*n* = 8)	All males (*n* = 19)
Age (years)	—	13.8±2.7	11.3±4.7	12.1±2.6	13.6 ± 5.2	12.7 ± 4.4
Thyroxine (μg/100 ml)	—	10.6 ± 5.1	6.4 ± 1.5	8.3 ± 1.4	7.7 ± 2.8	7.8 ± 3.0
TBC (μg/100 ml)	—	20.4 ± 3.9	22.4 ± 3.3	20.2 ± 0.6	19.7 ± 3.2	20.7 ± 3.2
TTBC (μg/100 ml)	—	31.0 ± 7.7	28.2 ± 3.3	28.5 ± 0.8	27.4 ± 4.3	28.3 ± 4.3
%TS	—	33.1 ± 9.6	23.0 ± 4.3	29.1 ± 4.1	27.8 ± 8.6	27.3 ± 7.5
EFT (ng/100 ml)	—	2.4 ± 1.1	1.3 ± 0.3	2.0 ± 0.4	1.9 ± 0.9	1.8 ± 0.8
Platelet MAO activity (nmoles/mg protein/hour)	—	30.6 ± 4.8	24.3 ± 3.5	30.2 ± 7.3	22.3 ± 5.8	25.1 ± 5.8

Table 2. Thyroxine indices and platelet MAO activity of females with thyroid disorders: Means and standard deviations

Variables	Simple goiter (*n* = 3)	Hyperthyroid (*n*=16)	Primary hypothyroid (*n*=7)	Euthyroid thyromegaly, thyroiditis (*n*=15)	Secondary hypothyroid (*n*=2)	All females (*n*=43)
Age (years)	14.6 ± 4.9	13.8 ± 2.7	11.4 ± 6.1	12.7 ± 2.9	14.1 ± 4.5	13.1 ± 3.6
Thyroxine (μg/100 ml)	6.8 ± 2.9	8.7 ± 3.4	9.5 ± 1.1	8.9 ± 3.6	9.0 ± 0.9	8.8 ± 3.1
TBC (μg/100 ml)	25.6 ± 2.9	21.1 ± 6.1	21.4 ± 2.6	22.5 ± 3.2	22.7 ± 3.0	22.1 ± 4.4
TTBC (μg/100 ml)	21.5 ± 18.7	30.2 ± 6.1	31.0 ± 3.5	31.4 ± 3.3	15.1 ± 21.3	29.4 ± 7.9
%TS	17.6 ± 15.6	27.4 ± 11.9	30.7 ± 2.3	28.0 ± 10.1	16.0 ± 22.6	26.9 ± 11.1
EFT (ng/100 ml)	1.3 ± 0.7	2.0 ± 1.1	2.1 ± 0.2	1.9 ± 1.1	1.9 ± 0.4	1.9 ± 0.9
Platelet MAO activity (nmoles/mg protein/hour)	32.4 ± 1.8	26.8 ± 7.9	30.9 ± 8.0	26.3 ± 7.3	31.1 ± 6.8	27.9 ± 7.5

ward a positive relation between platelet MAO activity and estimated free T_4 (Young et al. 1982); these associations were either absent or weakly present in patients with thyroid disorders. The female hyperthyroid group looked particularly different from the control group in these relations between platelet MAO activity and serum T_4 indices. The male patient groups were small, and there were no remarkable findings.

An earlier study investigated platelet MAO activity in hyperthyroid and hypothyroid patients who were symptomatic and characterized by laboratory measures of thyroid function outside the normal range. Most were not taking medication, and those who were being treated were reported to be receiving a medication that was said not to affect platelet MAO activity (propranolol). There was no alteration of platelet MAO activity in either of these patient groups

Table 3. Platelet monoamine oxidase activity and thyroxine indices in patients with thyroid disorders: Pearson correlation coefficients

Variables	Simple goiter	Hyperthyroid	Primary hypothyroid	Euthyroid thyromegaly, thyroiditis	Secondary hypothyroid	All male
Males						
Number	0	3	6	2	8	19
MAO—T_4	—	−.40	−.21	—	−.07	.04
MAO—TBC	—	.60	−.88[1]	—	−.52	−.26
MAO—EFT	—	−.63	.41	—	.14	.11
Females						**All female**
Number	3	16	7	15	2	43
MAO—T_4	−.04	−.23	.04	.33	—	.03
MAO—TBC	.47	.02	−.33	−.49	—	−.12
MAO—EFT	−.29	−.14	.49	.40	—	−.09

[1] $p < .05$

(Feldman and Roche 1977). Theoretically, thyroid disease is not the only potential source of a possible thyroid modulation of platetlet MAO activity; medications with strong effects on thyroid function might also elucidate thyroid regulation of MAO activity occurring outside the euthyroid range. Our results did not give any clear indication that there is a consistent relation between thyroid function and platelet MAO activity. The absence of results in this population may reflect the fact that nearly all the patients were well into treatment for their thyroid disease at the time of sample collection. A change in platelet MAO activity might be evident if a similar population were studied longitudinally from the time of diagnosis through treatment.

Thyroid hormone may have a significant regulatory impact on MAO activity in tissues other than platelets, for example, jejunal mucosa (Levine et al. 1962). Thyroid hormone is necessary for the synthesis of flavoprotein enzymes, such as MAO, as it enhances the conversion of riboflavin to the two flavin coenzymes, flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD) (Rivlin 1974). Thyroid hormone also stabilizes these flavoprotein enzymes, decreasing the rate at which they are degraded (Rivlin 1974). This role in stabilization is analogous to the action of glucocorticoids in stabilizing both dopamine-β-hydroxylase and phenylethanol N-methyltransferase, diminishing the rate of their degradation (Ciaranello 1978). This appears to be a general biological mechanism for the regulation of enzyme activity and further strategies should be considered in investigating thyroid-MAO interactions in humans.

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Catecholamine-Thyroid Hormone Interactions:

III. Serum DBH Activity and Thyroxine in Euthyroid Subjects

by J. Gerald Young, Richard M. Kyprie, and Donald J. Cohen

Abstract

Serum dopamine-β-hydroxylase (DBH) activity and thyroxine indices were examined in 76 children and adolescents with psychiatric disorders and normal control subjects. The negative relation between serum DBH activity and level of thyroid activity found in patients with thyroid disease did not hold when assessed in euthyroid subjects.

Dopamine-β-hydroxylase (DBH) is stored with norepinephrine (NE) in the granular vesicles of sympathetic nerve endings and the chromaffin granules of the adrenal medulla and catalyzes the formation of NE from dopamine. Both the enzyme and the reaction product are released proportionally into the serum with nerve stimulation. While serum DBH activity is not affected by adrenalectomy, it is reduced following "chemical sympathectomy" by 6-hydroxydopamine and in patients with diseases of the sympathetic nervous system (SNS) (Weinshilboum and Axelrod 1971*a*, 1971*b*; Noth and Mulrow 1976). The serum enzyme is biochemically similar to the enzyme present in sympathetic nerves and the adrenal medulla and has been suggested to be a convenient measure of SNS function (Schanberg and Kirshner 1976). Such pronounced sympathetic stresses as intense physical exercise, forced immobilization, and the cold pressor test induce an increase in serum DBH activity, while volume expansion (through albumin infusion) is accompanied by a decrease (Lamprecht, Williams, and Kopin 1973; Planz and Palm 1973; Wooten and Cardon 1973). Nevertheless, other sympathetic stresses do not cause similar changes in DBH activity, and there is no consistent relationship between DBH and indices of cardiovascular function, such as prevailing blood pressure. Study of the status of serum DBH activity as a marker of sympathetic activity is complicated by the large, genetically based, variation in serum DBH activity of up to 100-fold or more (Weinshilboum et al. 1976). Other sources of variance have been sought (Freedman et al. 1972).

Symptoms such as tachycardia, increased systolic blood pressure, sweating, and tremor in hyperthyroidism, and lethargy, bradycardia, and hypothermia in hypothyroidism, have suggested a thyroid-catecholamine interaction (Harrison 1964; Waldstein 1966; von Euler 1972; Spaulding and Noth 1975; Dratman et al. 1976). Biochemical substantiation has been based on a negative association between thyroid function and several catecholamine measures (Klawans and Shenker 1972; Christensen 1973; Stoffer et al. 1973; Cohen et al. 1974). A similar negative relationship between clinical thyroid status and serum DBH activity has been observed in patients with thyroid disease, with correction of the thyroid abnormality leading to return of DBH activity to the usual range (Noth and Spaulding 1974; Nishizawa et al. 1974).

We have studied thyroxine levels as a possible source of variance in serum DBH activity in a euthy-

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roid population with no known thyroid disease, consisting of children with psychiatric disturbances and control subjects.

Population and Methods

The population of 76 subjects ranged in age from 20 to 65 years (mean ± SD = 19.2 ± 13.4 years) and consisted of 57 males and 19 females. The 39 patients were children and adolescents (37 were male) with psychiatric disturbances. Each received extensive evaluations, and diagnoses were established according to *DSM–III* criteria (American Psychiatric Association 1980): childhood autism (21), developmental language disorder (5), and Tourette's syndrome (9). All patients were in good physical health; some patients were taking neuroleptic medication, but none of them were taking thyroid medication or any medication known to affect thyroid function. The 37 control subjects had no known medical or psychiatric illnesses and had taken no medication at the time of this study.

A 2 ml blood specimen was obtained by venipuncture and collected in a glass tube with no preservative or anticoagulant and allowed to clot for 15 minutes. Following centrifugation, the sample was stored at −20°C. The percent variation (calculated as $[(\Sigma x - x)/n]/x$) among seven samples assayed separately over 15 months was 5.2 percent. Serum DBH activity was measured according to the photometric method of Nagatsu and Udenfriend (1972) and reported as international units (µmoles octopamine formed/minute/l serum). Thyroxine (T_4, µg/100 ml) and residual thyroxine binding capacity (TBC, µg/100 ml) were measured, and the following values were derived: total thyroxine binding capacity (TTBC, µg/100 ml), percent thyroxine saturation of TTBC (%TS), and estimated free thyroxine (EFT, ng/100 ml) (Seligson and Seligson 1972, 1978).

Results

The mean DBH activity of the overall subject sample (*n* = 76) was 31.4 I.U., comparable to other subject groups. The mean levels of individual T_4 indices were all within the normal range (table 1) and were similar when subjects were divided by sex. No significant correlations were observed between serum DBH activity and serum T_4, TBC, or EFT (table 2). DBH activity was not related to T_4 indices for any of the three major diagnostic subgroups or when males and females were combined.

Table 1. Thyroxine indices of controls and patients with psychiatric disorders[1]

Variables	Control subjects (*n* = 37)	Patients (*n* = 39)	All subjects (*n* = 76)
Total thyroxine (µg/100 ml)	6.9 ± 1.3	6.7 ± 1.4	6.8 ± 1.4
TBC (µg/100 ml)	23.6 ± 3.2	22.3 ± 3.7	22.9 ± 3.5
TTBC (µg/100 ml)	30.3 ± 3.9	28.9 ± 4.2	29.6 ± 4.1
%TS	22.3 ± 3.2	23.1 ± 4.4	22.7 ± 3.9
EFT (ng/100 ml)	1.3 ± 0.3	1.4 ± 0.4	1.4 ± 0.3

[1] Mean ± SD.

Table 2. Serum DBH activity and T_4 indices in children with psychiatric disorders and controls: Pearson correlation coefficients

Variables	Control subjects	Patients	All subjects
Males			
Number	20	37	57
DBH–T_4	.11	−.15	−.04
DBH–TBC	.39	.01	.15
DBH–EFT	−.13	−.17	−.15
Female			
Number	17	2	19
DBH–T_4	−.36	—	−.33
DBH–TBC	−.24	—	−.25
DBH–EFT	−.15	—	−.11

Discussion

Our study did not demonstrate an association between serum DBH activity and T_4 indices in normal controls or children with psychiatric disorders. The previously reported negative association between DBH activity and T_4 (Nishigawa et al. 1974; Noth and Spaulding 1974) appears to occur only outside the range of normal thyroid function in cases of thyroid disease. Thyroid function apparently is not a major source of the large variation in DBH activity in normal, euthyroid subjects. However, it must be considered that a negative association might have been obscured by this genetic variance in enzyme activity. The importance of understanding this relation suggests that it should be investigated in a larger population and in other groups of patients.

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Cognitive and Emotional Functioning in Hypopituitary Short-Statured Children

by Deborah Abbott,
Diane Rotnem,
Myron Genel,
and Donald J. Cohen

Abstract

Eleven children with documented growth hormone deficiency were studied to assess their cognitive and emotional functioning and their academic achievement before and after 1 year of human growth hormone replacement therapy. Standardized personality and intelligence measures were used, and records of school achievement, as well as developmental and family history from parents, were obtained. Although some subjects in this group were coping with problems other than their short stature (e.g., other medical and psychosocial problems), their intelligence and academic achievement were found to be positively correlated with socioeconomic status and independent of the condition of hypopituitarism. This study supports others that have found these children vulnerable to problems of emotional adjustment in middle and late childhood. Because of the heterogeneity of the group, findings must be interpreted cautiously. However, the consistent finding of disturbance in visual-motor integration is thought to be significant and demonstrates the need for further research that will examine possible neurological sequelae of long-term growth hormone deficiency.

Problems of coping with short stature have been well described in various populations of children with hypopituitarism (Green, Schur, and Lipkowitz 1959; Kusalic and Gauthier 1972; Schwartz and Sturges 1973; Rotnem et al. 1977, 1979). However, in the past, descriptive clinical investigations have led to more controversy than agreement concerning the etiology of personality and cognitive difficulties in this vulnerable population (Drash, Greenberg, and Money 1968; Krims 1968). Findings concerning emotional and intellectual functioning have varied from study to study, perhaps because of the heterogeneity of the populations studied (Kusalic 1975; Steinhausen and Stahnke 1976; Steinhausen 1977).

Issues of psychomaturation in relation to social and coping behavior, as well as cognitive development, have been addressed by psychoendocrine researchers (Money, Drash, and Lewis 1967; Frankel and Laron 1968; Money and Poliitt 1968; Pollitt and Money 1968; Kusalic and Fortin 1975; Brust, Ford, and Rimoin 1976). Most studies have emphasized social-environmental influences affecting the child's psychological response to his growth handicap, and therefore his personality and cognitive functioning (Spencer and Raft 1974; Steinhausen and Stahnke 1976; Steinhausen 1977). Others have found it relevant to consider the potential impact of disruption in endocrine and central nervous system (CNS) maturation (Cleghorn 1973; Cohen 1975; Martin 1973; Cohen and Frank 1976; Rotnem et al. 1977, 1979). The relationship between the possible biochemical aberrations and the possible social-emotional influences on problems associated with hypopituitary short stature is poorly understood.

There is some consensus in the

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recent literature that social-emotional adjustment and achievement vary with the populations studied (Steinhausen and Stahnke 1976). When serious psychopathology is present in the children, it also tends to be present in the families, thereby suggesting an environmental influence (Pollitt and Money 1964; Kusalic and Fortin 1975). Similarly, the stability of the family unit (Love 1970; Schwartz and Sturges 1973) and parenting success in treating the child with age-appropriate behavioral expectations have been seen as major determinants of good overall adjustment to the psychosocial problems of short stature (Drash, Greenberg, and Money 1968; Schwartz and Sturges 1973; Rotnem et al. 1977, 1979).

Intelligence has been generally recognized as independent of statural growth (Money, Drash, and Lewis 1967; Steinhausen and Stahnke, 1976). It has been found by most researchers to fall in the average range (Money, Drash, and Lewis 1967; Drash, Greenberg, and Money 1968; Meyer-Bahlburg et al. 1978). Borderline and low average IQ scores in hypopituitary short-statured children have been related to low parental expectations and unavailability of remedial tutoring required by some groups of children (Frankel and Laron 1968; Shurka and Laron 1975). While school achievement has been described as characteristically poor in children who have short stature secondary to pituitary dysfunction (Pollitt and Money 1964; Money and Pollitt 1968), the studies in this area suggest strong social-emotional influences, rather than poor intellectual endowment. For example, the child's need to direct his energy toward social activities and peer group acceptance may take precedence over a drive for scholastic achievement (Brust, Ford, and Rimoin 1976). In some studies, good school adjustment and scholastic achievement have been shown to be a method of gaining acceptance from peers at the actual, rather than the apparent, age level (Rosenbloom, Smith, and Loeb 1966).

The Yale studies on psychological and intellectual development of short-statured children were initiated more than 15 years ago (Schwartz and Sturges 1973). Since 1970, 50 children have been studied metabolically and treated with human growth hormone (hGH) replacement. Twenty-five children have received detailed, multidisciplinary evaluation of psychological, familial, and behavioral functioning (Rotnem et al. 1977, 1979). In previous studies, we have found that hypopituitary children show a predisposition to psychomaturational difficulties, particularly in areas of self-esteem regulation, socialization, and modulation of aggression. Many children have disturbances in mood, most notably depression, and this underlying predisposition may be exacerbated during hGH treatment by the unrealistic expectations they have that this treatment will make them completely normal (Rotnem et al. 1977, 1979).

We now present a new group of 11 children, not previously described, and replicate and extend our previous findings by more detailed evaluation of cognitive and emotional functioning. The psychological development of hypopituitary children is a good model of the interaction between biological and environmental factors in the emergence of social competence in childhood (Talbot et al. 1947).

Description of Study

Subjects. The sample of 11 subjects consisted of four girls and seven boys who ranged in age from 4 to 18 years (mean ± SD = 11.1 ± 3.11 years) at the time of pretesting. Nine lived with their own families, two with foster families. Six lived in intact families, five in one-parent families.

Four children had isolated growth hormone deficiency, four had panhypopituitarism, and three had isolated growth hormone deficiency with other serious medical problems (table 1). The heterogeneity of the cohort presents dilemmas familiar to clinical investigators but renders analysis of the results more complicated and the conclusions more tentative.

Methods. The children were admitted to the Children's Clinical Research Center for metabolic evaluation of pituitary function before the initiation of human growth hormone (pretesting), and approximately 1 year after initiation of the treatment (posttesting). Pituitary function was assessed in all subjects using standard endocrinologic procedures (Milewski et al. 1975; Rotnem et al. 1977). Children were admitted two or three at a time and matched by age and sex in order to provide peer support. Following endocrinologic evaluation, subjects were started on hGH replacement at a dosage of 0.30 U/kg/week or 0.15 U/kg/week in three divided intramuscular injections weekly. At periodic clinical

Table 1. Pretest subject data

Subject	Age	Sex	Race	SES	Height (in cm)	Height age[1] (years)	Bone age (years)	Diagnosis/hormone deficiencies
A	4.4	M	W	M	81.0	1.5	2.11	Isolated growth hormone deficiency
B	6.1	M	W	M	93.0	2.1	4.5	Isolated growth hormone deficiency
C	7.2	M	B	L	100.5	3.8	2.1 to 4.0	Panhypopituitarism
D	7.5	F	B	L	97.8	3.5	3.2	Panhypopituitarism
E	8.10	F	W	L	88.1	2.3	5	Congenital goiter and growth hormone deficiency
F	11.8	F	W	H/M	117.2	6.4	6	Isolated growth hormone deficiency
G	12.3	F	W	M	120.0	6.10	8	Isolated growth hormone deficiency
H	12.5	M	W	L	121.2	6.11	9	Panhypopituitarism
I	16.7	M	W	M	131.0	8.9	12	Isolated growth hormone deficiency Esotropia, nystagmus, and severe myopia
J	17.6	M	W	M	132.2[2]	9.0	13.6	Panhypopituitarism
K	18.0	M	W	M	130.1[3]	8.7	13[4]	Panhypopituitarism and complex congenital heart disease with mid-line facial defect

[1] Charts: Ross Laboratories, National Center for Health Statistics, NCHS Growth Charts, 1976. Monthly *Vital Statistics Report*, Vol. 25, No 3 Supp. (HRA) 76–1120. HA plotted on the 50th percentile.

[2] Six-week followup.

[3] At 17.8 years of age.

[4] At 18.3 years of age.

evaluation, status and growth were assessed.

Data on intellectual and emotional functioning were obtained by means of standardized psychological tests administered by a clinical psychologist (D.A.). The following instruments were used: Developmental Test of Visual-Motor Integration (Beery); one form of the Wechsler Intelligence Scale (WPPSI, WISC-R, or WAIS); the Wide Range Achievement Test (WRAT); Draw-a-Person (male and female drawings); the Kinetic Family Drawing; the Rorschach Inkblot Test; and the Tasks of Emotional Development (TED) Test (Cohen and Weil 1971*a*, 1971*b*). The TED is a personality test similar to the Thematic Apperception Test. It consists of a sequence of cards, each of which is designed to assess the child's coping with age-appropriate developmental tasks (Cohen and Weil 1971*a*, 1971*b*). In addition, the Bender-Gestalt Test was included in the posttesting. Finally, the psychologist completed the Childhood Personality Scale (CPS-R) for each subject after pretesting and posttesting (Dibble and Cohen 1974; Cohen, Dibble, and Grawe 1977).

In addition, parents were engaged in a semistructured clinical interview with a pediatric research social worker (D.R.) during the first admission. The interview focused on parental perceptions of the child's medical problem and overall social-emotional adjustment, as well as developmental history on each subject including parent and sibling relationships. Each parent completed the CPS-R and standardized questionnaires which related to family background, their child's personality, developmental history, and recent family changes. School records were requested for each subject.

Results

Intellectual Functioning. Results of the Wechsler, Beery, DAP, and WRAT indicate that the group's verbal, nonverbal, and overall abilities fall within the "low average" range (table 2) with no significant differences between pretest and posttest IQs. Parent occupational levels in our sample included more subjects of low socioeconomic status (SES) and fewer of high SES than the sample studied by Wechsler (WISC-R, 1974). Given this difference, mean IQs of our sample would be expected to fall somewhat below average.

Results of the Beery, DAP, and Bender indicate that the group's visual-motor integration skills were significantly below average (table 3). Furthermore, performance was significantly poorer on posttesting than on pretesting (Beery: $t = 3.1$, $p < .01$; DAP: $t = 2.5$, $p < .02$). Discrepancies between chronological age and developmental age increased with age. For instance, the correlation between age and Beery scores on posttesting was significant ($r = 0.69$, $df = 10$, $p < .025$). The older the subject, the poorer the performance. Furthermore, a relatively clear-cut sex difference appeared, with boys as a group scoring lower than girls as a group. However, the four oldest subjects were boys. If this factor and the tendency for scores to become poorer with increasing age are taken into account, it is not possible to determine whether age or sex is more of a contributing factor to the inferior performance of the group.

The results of these three paper-and-pencil tests did not appear to be a function of IQ; there were no significant correlations between IQ scores and these measures (e.g., the highest correlation was $r = 0.53$, $df = 10$, for the Beery and the PIQ). There were, however, significant correlations among the scores of the visual-motor integration measures on both pretesting and posttesting administrations. The correlations were at the .005 level and beyond (Beery, DAP: pre: $r = 0.88$; post: $r = 0.88$; Beery, Bender: post: $r = 0.85$).

The WRAT standard scores on pretesting and posttesting for reading, spelling, and arithmetic were compared with each other

Table 2. Wechsler Intelligence Scale for Children—Revised

IQ	Pretest[1]	Posttest[1]
Verbal IQ	89.3 ± 19.8	86.4 ± 22.8
Performance IQ	89.2 ± 16.1	87.2 ± 22.6
Full-scale IQ	88.2 ± 17.2	85.6 ± 23.8

[1] Mean ± SD.

Table 3. Discrepancy between chronological age and age equivalencies (in years and months)

Measures	Pretest	Posttest
Beery		
All subjects	2.5 (2.0)[1]	3.8 (3.3)[1]
Males	3.2 (2.7)[1]	5.0 (4.0)[1]
Females	1.2	2.1
Draw-a-Person[2]		
All subjects	3.9 (3.3)[1]	4.7 (4.1)[1]
Males	4.1 (3.8)[1]	4.5 (3.8)[1]
Females	2.8	4.9
Bender		
All subjects	—	2.1 (2.2)[1]
Males	—	2.2 (1.5)[1]
Females	—	1.8

[1] Excluding I, subject with visual defect.
[2] First of two drawings (Harris scoring system).

and with the full-scale IQs (table 4). The results indicate that the group's achievement was in the low average range, compatible with its potential as measured by the Wechsler (positive correlations from $r = .51$ to .76). School performance determined from school records was variable. Five of 11 subjects had been retained at least one grade in school, four due to absenteeism from serious illnesses and hospitalizations. Five subjects performed at or above average in school. Achievement generally decreased with chronological age.

In summary, the data on intellectual functioning indicate the following:

- IQs for the group as a whole fell in the high end of the "low average" range.
- Overall IQ was more related to SES level and specific physical dysfunction such as eye defect or congenital goiter than to the condition of hypopituitarism.
- The group reflected deficits in visual-motor integration skills on paper-and-pencil tasks.
- Scatter within IQ scores and particularly deficits in visual-motor integration ability might be associated with the long-term effects of growth hormone deficiency.
- Lowered academic achievement was associated with lower than average IQ, and possibly with deficits in visual-motor integration ability.

Table 4. Wide Range Achievement Test (WRAT)

Measures	Pretest[1]	Posttest[1]
Full Scale IQ	88.2 ± 17.2	85.6 ± 23.8
Reading	88.4 ± 16.9	95.0 ± 17.6
Spelling	85.2 ± 13.8	92.6 ± 16.4
Arithmetic	82.6 ± 15.1	81.3 ± 19.0

[1] Mean ± SD.

Emotional Functioning. Emotional adjustment of each subject was assessed by the psychologist on the basis of test data (TED, Rorschach, DAP, KFD) and observations of subjects during research hospitalization. Children's abilities to cope adaptively with problems of realistic concern were assessed, rather than the presence or absence of problems themselves. For example, it was assumed that an 18-year-old male with delayed puberty would have serious problems with sex role identification, peer relationships, and self-esteem. However, his emotional adjustment was not considered to be poor unless he was coping poorly with these realistic concerns.

As with overall IQ scores, the general level of emotional adjustment did not appear to be dependent on the hypopituitarism, as such. Similarly, the results for the group as a whole on the CPS did not indicate extremes in the areas of attention, behavior modulation, socialization, zestfulness, or emotional expressiveness. On the basis of the examiner's ratings, two subjects were felt to have severe emotional problems; two, moderate problems; six, minor problems; and one, no significant problems. There was no evidence of overt thought disorder, schizophrenia, or borderline personality. However, the children appeared prone to low spirits and depression. Furthermore, general emotional adjustment did not appear to be dependent on SES or IQ levels, and was not age- or sex-related. However, there were suggestions that complicating medical or family events were important factors in the level of emotional adjustment (e.g., frequent hospitalizations, loss of a parent through death or divorce).

Level of maturity and concept of self within the context of the family have been noted to be important variables in earlier clinical studies (Kusalic and Gauthier 1972; Kusalic and Fortin 1975; Rotnem et al. 1977, 1979). Subjects' responses to the TED cards were the primary source of testing data on level of maturity. TED card responses were scored independently by the psychologist and social worker. Interrater reliabilities were assessed by use of the weighted kappa (Cohen 1968; Cicchetti 1976) and were acceptable for ratings of perception of 11 of 13 cards and for ratings of outcome on 8 of the 13 cards (.6 or better). Disagreements were discussed and resolved on all but one rating. Final ratings were then made (table 5) using test manual norms.

Results suggested that the group as a whole was likely to perceive developmental tasks as accurately as normal and clinic samples, but was less likely to cope with them successfully (table 5). In this sense, the hypopituitary children were immature. For example, adolescents did poorly in dealing successfully with the card related to positive heterosexual socialization, although they perceived the task accurately.

In contrast to hypopituitary children described in previous studies as struggling with feelings of isolation within the peer group (Schwartz and Sturges 1973; Rotnem et al. 1977, 1979), this group tended to be quite well adjusted in reciprocal friendships with peers. Finally, the group tended to have a negative attitude toward learning and experienced conflicts in the areas of identification with the same-sex parent, establishment of a conscience, and ambivalence toward siblings. All subjects were aware of their small stature, and even the most well-adjusted communicated a sense that others perceived a babyish quality to their appearance, thus leading to conflict in the establishment of a positive self-concept. There was also difficulty in the acceptance and control of aggressive feelings toward peers. In general, the group could perceive a potential fight with a peer but tended to respond with sadness or fear rather than with retaliation.

Perception of self and family was evaluated on the basis of the DAP and KFD, as well as TED and interview data. The drawings suggested that children had formed at least a partial appropriate sex identification. They often depicted themselves in family drawings as a small figure, regardless of their age compared to siblings. However, most children drew heads of their figures proportionately larger for the bodies than is considered appropriate. They often included and identified with a younger member of the family or extended family, typically a baby. This tendency was highlighted in the behavior of children when they assumed a pseudo-adult "parenting" role with a particular baby on the ward. Many presented their families as positive aspects of their lives; although they felt small and vulnerable, they typically portrayed themselves as integral parts of a family unit, valued by other members. Feelings of acceptance within their families were validated by observation, interviews with both children and families, and the Kinetic Family Drawing.

A tendency to deny the short stature was present in all parents at one stage or another. In the three children who had other associated and serious medical problems, parents considered their child's short stature to be the least of his or her problems. In all cases, fathers had more difficulty accepting the diagnosis than mothers.

Most parents saw their child's main difficulties as the following:

- Feeling less competent than younger siblings who were taller;
- Teasing by peers, such as name calling, scape-goating, avoidance;
- Wishing to be babied.

Discussion

The results of research on psychological aspects of hypopituitarism have been inconsistent, although more so in descriptions of emotional than intellectual functioning. Based on previous work and our own research, we would

Table 5. Tasks of Emotional Development (TED) Test: Perception of task and perception of outcome (by percent)

Card	Developmental task	Card description	Correct perception of task (%)	Correct perception of successful outcome (%)
1	Peer socialization	Group of children on one side with single child off to other side	100	82
2	Establishment of trust	Woman holding bowl out to child	64	64
3	Acceptance of aggressive feelings	Two children with fists raised	73	40
4	Positive attitudes toward learning	Child sitting at desk	82	73
5	Establishment of a conscience	Child looking at wallet left on table	60	10
6	Separation from mother	Child standing by door looking at woman	73	73
7	Sexual identification	Man and woman standing at kitchen counter with child looking on	90	60
8	Acceptance of siblings	Woman holding baby with child looking on	91	45
9	Acceptance of limits	Woman with hand on TV switch with child looking on	64	45
10	Acceptance of affection between parents	Man and woman embracing with child looking on	91	80
11	Establishment of orderliness	Woman pointing to pile of clothes on floor with child looking on	100	88
12	Establishment of self-concept	Child looking in mirror at reflection of himself	80	50
13	Heterosexual socialization	Boy walking up sidewalk to girl's house	33	33
Mean			77	77

like to consider some possible explanations for the inconsistencies and offer guidelines for future research.

First, some researchers report average (e.g., Pollitt and Money 1964; Drash, Greenberg, and Money 1968) and some report below average IQ scores (e.g., Shurka and Laron 1975). However, it appears in all studies that the overall intellectual ability of hypopituitary children appears to be more dependent on socioeconomic status than on the condition of hypopituitarism (Steinhausen and Stahnke 1976).

Second, some researchers report average and above average academic achievement (Pollitt and Money 1964; Shurka and Laron 1975), and some report below average academic achievement (Rosenbloom, Smith, and Loeb 1966; Schwartz and Sturges 1973). It appears that a combination of factors determines level of achievement in the various samples (e.g., level of intellectual ability, stability of family, and support of the educational system). Once again, it does not appear that achievement is related to the condition of hypopituitarism but, rather, is compatible with intellectual potential (IQ) as measured on the Wechsler. However, the question of cognitive inhibition secondary to depressive symptomatology cannot be ruled out.

Third, evidence of a possible defect in visual-motor integration ability has been reported recently (e.g., Frankel and Laron 1968; Shurka and Laron 1975; Steinhausen and Stahnke 1976). Our research indicates a lag in the development of visual-motor integration skills on paper-and-pencil tasks.

Fourth, diverse findings have been reported in areas of emotional functioning (Meyer-Bahlburg 1978). While most children with hypopituitarism have adjustment difficulties, the difficulties range from reports of fairly adequate adjustment (e.g., Pollit and Money 1964; Drotar, Owens, and Gotthold 1980) to reports of psychotic depression (Hanna 1970; Kusalic and Fortin 1975). Our findings suggest that adjustment problems in school, family, and peer groups are significant among this group of children, but relatively characteristic of any child and family where there is chronic illness. For these children, those difficulties center around the following issues: concerns about bodily integrity, vulnerability within a peer group, desire for acceptance, and academic achievement. Pre- and early adolescence are particularly difficult periods since it is then that the greatest disparity between the hypopituitary short child and his peer group is evident.

The diversity in adjustment of subjects in our studies appears to relate more to socioeconomic status, family stability, the family's attitude toward a short-statured child, and school and peer responses than to the hypopituitarism itself. These children should be considered particularly at risk for developmental difficulties in middle and late childhood, but to have potential strength for coping on the basis of relatively normal early experience. Our results indicate that adolescence is the most problematic stage, and that hypopituitary children are more vulnerable to depression than acting-out disorders.

On the basis of cognitive and personality testing and parent interviews, the present group appeared generally better adjusted than the previous groups we have studied. This result may reflect actual differences between the samples, as well as better informed pediatricians who refer and diagnose children earlier and offer better and more realistic preparation for parents and children for the limitations of growth hormone treatment.

The most significant finding of this study is the deficit in visual-motor integration skills on paper-and-pencil-tasks. This area requires further exploration and clarification. Future studies of the specific nature and etiology of dysfunctions of visual-motor integration in hypopituitary children should address the presence or absence of specific learning disabilities and specific visual and kinesthetic-motor functioning disturbances. The present results can be considered only tentative due to the small sample size and heterogeneity of medical diagnoses and environments. There is still a need to understand possible neurological sequelae of long-term growth hormone deficiency. Finally, future research should attempt to follow children longitudinally and assess young adult functioning in areas of education, vocational training, and social adjustment.

The history of children with hypopituitary short stature reveals the ways in which school-aged children and their families cope with a chronic disease that has obvious physical and social stigmata. Earlier diagnosis and the markedly increased availability of growth hormone, as a result of genetic engineering, will likely bring more hypopituitary and other short children to diagnosis and treatment. The careful study of the psychological significance of short stature and its remediation can provide further information on the role of bodily integrity and family functioning in the mental lives of hypopituitary children.

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Efficacy of Neuroleptic Medication in Pervasive Developmental Disorders of Childhood

by Edwin J. Mikkelsen

Abstract

A number of studies pertaining to the use of antipsychotic medication in the treatment of pervasively disordered children are reviewed. The drugs examined are chlorpromazine, haloperidol, thioridazine, thiothixene, trifluoperazine, lithium, and other miscellaneous agents. Medication side effects are also reviewed with particular attention to extrapyramidal symptoms and tardive dyskinesia. Although methodological problems complicate the interpretation of the studies, the results support the use of antipsychotic medication in this population. The agents do not have the specificity for psychotic ideation that is seen in adult patients, but are useful for symptoms such as hyperactivity, stereotyped behavior, aggressiveness, impulsivity, self-abusive behavior, and social adaptation.

The extension of the use of neuroleptic medication from psychotic adults to severely disturbed children has provided interesting data on clinical utility and insights into the relationship between the severe behavior disorders of childhood and the adult psychoses. The confusion surrounding the diagnosis of the severely disturbed child is mirrored in the pharmacological studies that have been carried out in this population. The principal groups that have been studied are childhood schizophrenia, infantile autism, the mentally retarded, and the hyperkinetic-learning disabled. However, it is often difficult to discern which of these populations, or which mixture of these populations, was studied in the experiments reported. This difficulty stems in part from the fact that studies done before publication of *DSM-III* (American Psychiatric Association 1980) used *DSM-II* nomenclature, which placed autistic children under the classification of schizophrenia.

Despite these methodological problems, the literature provides some consensus, as well as practical information for clinicians who prescribe psychotropic drugs to disturbed children.

Clinical Studies

In a thorough review of studies dealing with the use of psychotropic medication in severely disturbed children, Magda Campbell (1975) identified the following factors as important ingredients for a successful study:

- Differentiation of drug effects from effects of environmental manipulation.
- Control of variables that are likely to influence outcome (age, diagnosis, severity, IQ, social class).
- Placebo washout.
- Proper assessment of baseline behavior.
- Double-blind design with random allocation of patients.
- Determination of appropriate dose range.
- Appropriate attention to order effects.
- Adequate number of trained, independent observers.
- Standardized, sensitive, and population-appropriate meas-

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ures of change to permit communication among investigators.
- Limited length of drug administration in order to differentiate drug-induced changes from maturational changes.
- Tabular or graphic presentation of data.

In addition, one needs to stress the importance of determining not only appropriate dosage ranges, but also of establishing reasonable equivalency doses when two or more drugs are compared. For example, as Winsberg and Yepes (1978) note, Ucer and Kreger's (1969) finding that haloperidol is superior to thioridazine in the treatment of mentally retarded children is difficult to interpret because proportionally higher doses of haloperidol than of thioridazine were used in the study.

Another point stressed by Campbell (1975) is the need for careful diagnostic selection and uniform rating scales. In many studies, it is almost impossible to identify the diagnostic group under investigation. Terms such as "psychotic-retarded-autistic" are not uncommon in the methods sections of these studies. In the main, subjects comprise those who suffer from psychosis, autism, mental retardation, or extreme hyperactivity with developmental delay. The lack of diagnostic precision apparent in many studies mirrors the state of diagnosis in clinical practice. It also reflects the fact that many of these pervasively disordered children have multiple problems. For example, it is not uncommon for a mentally deficient child to have a concomitant psychosis and to be quite hyperactive. Experienced clinicians often cannot agree on whether the proper diagnosis for a given child is mental retardation or autism. It is to be hoped that advances in the coming years will make possible the assignment of these disturbed children to clinically relevant subgroups. For the time being, diagnostic problems can be minimized by using uniform rating scales and by using effects on a given target symptom to assess drug efficacy. This is in contradistinction to the approach used in many of the studies reviewed here which consisted of studying changes in broad diagnostic groups by means of global behavioral ratings.

Pharmacokinetics

Before studies dealing with individual drugs are reviewed, mention must be made of our current understanding of the pharmacokinetics of these drugs.

In their review, Winsberg and Yepes (1978) note that no studies of pharmacokinetic data in children have yet been reported. They indicate that differences from adults would likely be "quantitative rather than qualitative." In a recent case study, Meyers, Tune, and Coyle (1980) measured clinical response to haloperidol in relation to blood level and suggested that the dose-response relationships were similar to those in adults. Campbell et al. (in press) carried out a placebo-controlled, double-blind study of haloperidol in 33 autistic children, aged 2.3 to 7.9 years. The authors reported that, at the clinically optimal haloperidol dosage of 0.5 mg/day to 3.0 mg/day, the serum levels of haloperidol ranged from not detectable (less than .05 ng/ml) to 8.30 ng/ml. Peak blood levels for most of the antipsychotic medications occur within 1 to 4 hours after administration (Winsberg and Yepes 1978). While the range in half-life for chlorpromazine is great between subjects, it is well within 6 hours for 80 percent of the subjects in a study by Curry (1968). The half-life figures for thioridazine (24 hours) and haloperidol (12–38 hours) are somewhat longer. Brain concentrations are usually thought to be higher than blood concentrations because of the lipid solubility of the drugs. The drugs have metabolites, ranging from over 150 for chlorpromazine (Curry 1968) to a few for haloperidol, some of which may be psychoactive. Due to storage and subsequent slow release, the drug may be excreted for several weeks after a prolonged course of medication. Accordingly, it may take several days before the clinical effects of the medication begin to wane.

Specific Agents

While a large number of antipsychotic agents have been tried in children, only a few have been the subject of systematic investigation.

Chlorpromazine

Since chlorpromazine was the first antipsychotic agent introduced, it is not surprising that the earliest studies in children involve its use. Three years after the introduction of chlorpromazine, Freedman, Effron, and Bender (1955) carried out a placebo-controlled study with schizophrenic children and found significant effects at doses of 30 to 100 mg. In an interesting, early, uncontrolled study, Hunt, Frank, and Krush (1956) found that acute onset schizophrenic adolescents had a much better response to the medication than did those whose illnesses began in childhood. This finding suggests that the two illnesses may be distinct disease entities, rather than different points on a common continuum.

In a followup of two earlier studies, Fish (1960), Fish et al. (1969*a*), and Campbell et al. (1972*c*) compared "sedative" neuroleptics such as chlorpromazine and "stimulating" agents such as trifluperidol. In a study of 15 hospitalized children, trifluperidol was found to be significantly more effective than chlorpromazine or placebo. The primary drawback to chlorpromazine was its sedative effect, which tended to increase the hypoactivity of the more anergic children. This finding is in keeping with the observation of Freedman, Effron, and Bender (1955) that chlorpromazine was more useful for the hyperkinetic, agitated, psychotic child.

Engelhardt, Polizos, and Margolis (1972) carried out an extensive series of studies in children diagnosed as suffering from childhood schizophrenia or early infantile autism. The drugs compared were chlorpromazine, thioridazine, trifluoperazine, prochlorperazine, and fluphenazine. Chlorpromazine was less effective than anticipated; although children treated with chlorpromazine became more manageable, the investigators did not observe the specific antipsychotic effect seen in adult schizophrenia. In a diagnostically mixed population, Fish and Shapiro (1965) found chlorpromazine to be substantially better than placebo in severely disturbed children; among children who were less disturbed, however, 60 percent responded to chlorpromazine, while 43 percent responded to placebo. Because the sample size in this study was modest, no definite conclusions can be drawn.

Chlorpromazine has also been extensively studied in the emotionally disturbed, mentally retarded population. Winsberg and Yepes (1978) have reviewed the literature and note that chlorpromazine consistently has been found to decrease hyperactivity and abnormal or bizarre behaviors. However, many of the studies have been poorly controlled.

A special concern in the use of antipsychotic medications is the possibility that they might adversely affect learning. Alternatively, one might hypothesize that, if the drugs were effective in treating an underlying thought disorder, then a child would be better able to concentrate, and his academic performance might actually improve. An early study by Freed, Abrams, and Peifer (1959) provided support for the latter contention: Chlorpromazine and reading instruction were found to be superior to instruction alone in children with marked reading delays. A later study by Freibergs, Douglas, and Weiss (1968) evaluated the effects of chlorpromazine (average dose, approximately 100 mg/day) versus placebo in 36 hyperactive boys. The authors concluded that the drug was moderately successful in controlling hyperactivity without having an adverse affect on learning ability or other psychological functions. In a more rigorous study conducted on 39 children hospitalized because of "severe emotional disorders," Helper, Wilbott, and Garfield (1963) found that chlorpromazine had an adverse effect on paired-associate learning and that this effect was more pronounced in those subjects who initially learned more slowly. Porteus Maze scores also declined, but no drug effect was noted on remote or immediate memory. In keeping with the above-noted more pronounced effect on the slower learners, Hollis and St. Omer (1972) found that chlorpromazine depressed conditioned motor behavior in a population of mentally retarded children.

Thus, chlorpromazine does appear to have subtle, deleterious effects on learning in children—effects that may be more pronounced in those children with decreased intellectual functioning.

Haloperidol

Haloperidol has also been relatively well studied. An uncontrolled study by LeVann (1969) found it useful in schizophrenic children, as did a placebo-controlled study by Barker and Fraser (1968) of 16 moderately-to-severely disturbed children with heterogeneous diagnoses. In the latter study, haloperidol proved significantly superior to placebo at dosages below 0.1 mg/kg. Only global ratings were used, however, and the population was quite heterogeneous.

Ucer and Kreger (1969) compared haloperidol with thioridazine in a double-blind study of emotionally disturbed, retarded children. In their sample of 26 children (ages 7 to 12; IQ 40 to 70), they found that haloperidol produced moderate-to-marked improvement (as assessed by global ratings) in 54 percent of the children, whereas only 21 percent of the thioridazine group improved to this degree. Haloperidol was also more useful for individual target symptoms such as hyperactivity and impulsivity. As Winsberg and Yepes (1978) have pointed out, however, the interpretation of these results is confounded by the fact that the mean haloperidol dose was 2.25 mg and the mean thioridazine dose was 53 mg, so that the children received proportionately more haloperidol on a milligram-potency basis. Haloperidol and thioridazine proved equally effective in a double-blind study using more equivalent dosages of the medications in a population of 63 children with heterogeneous diagnoses (Claghorn 1972).

Lewis and James (1973) compared haloperidol (.05 mg/kg twice daily) to chlorpromazine (2.5 mg/kg twice daily) in 31 children (many adolescents) who were disturbed enough to warrant hospitalization. The four major diagnostic groups were neurosis, psychosis, situational disorder, and unspecified behavior disorder. The authors devised a 10-item assessment scale with a 4-point ordinal scale for each. This study failed to show any statistical advantage for either chlorpromazine or haloperidol in the dosages described above as compared to placebo; however, there was a significant correlation between improvement and positive changes in the parent-child interaction.

Three studies have compared haloperidol to fluphenazine. In a double-blind study by Serrano and Forbis (1973) of 30 children aged 6 to 11, with diagnoses ranging from nonpsychotic organic brain disorder to adjustment reaction of childhood, haloperidol (.5 to 2 mg) acted more rapidly and also was associated with greater global improvement than fluphenazine (1 to 4 mg). Haloperidol was also more effective in improving ratings in a social behavior symptom cluster and an affective cluster. Both drugs were equally effective in decreasing hyperactivity. Faretra, Dooher, and Dowling (1970) also compared the two agents in double-blind, parallel trials of the drugs in populations of 30 each. More than 80 percent of the children in each cohort were given diagnoses of childhood schizophrenia. Dosages employed were identical for both drugs at 0.25 mg three times a day titrated upward to 1.25 mg three times a day. Although global ratings associated with the two drugs did not differ significantly, haloperidol appeared to have an earlier effect. Haloperidol was also somewhat more beneficial for many of the target symptoms studied. Interestingly, both drugs tended to produce better results at 4 weeks, than at 8 weeks, suggesting that the 4-week dose of 0.25 mg three times a day may have been more effective than the 1.25 mg t.i.d. dose used at 8 weeks. Engelhardt et al. (1973) also conducted a double-blind study comparing fluphenazine and haloperidol in 30 outpatient schizophrenic children who ranged in age from 6 to 12. The mean dose for both drugs was 10.2 mg/day, with a maximum dose of 16 mg/day. The drugs were found to be equally effective in terms of overall improvement; fluphenazine produced slightly more extrapyramidal symptoms than did haloperidol.

As with chlorpromazine, the possibility that haloperidol could cause significant cognitive blunting or impairment in learning is a major concern. In a well-controlled study comparing high dose (0.05 mg/kg/day) and low dose (0.025 mg/kg/day) haloperidol to methylphenidate (0.3 mg/kg) and placebo in 24 hyperactive, aggressive children (ages 4 to 12), Werry and Aman (1975) found that the low dose of haloperidol actually facilitated performance on measures of attention and memory, while the high dose of haloperidol decreased performance. Although this decrement was found on only one task, the finding was compatible with two earlier studies. Wong and Cock (1971) found little impairment of cognitive functioning using doses of 0.05 mg/kg, whereas Cunningham, Pillai, and Roger (1968), using doses of 0.10 mg/kg, found definite psychomotor slowing.

In the best study to date, Campbell et al. (in press) found that, at optimal clinical doses (0.5 mg/day to 3.0 mg/day), haloperidol facilitated learning in autistic children in an operant-conditioned discrimination task. The children receiving haloperidol did much better than those on placebo. In the crossover situation, the haloperidol effect continued when the children were placed on placebo; those children who were first on placebo showed improvement on haloperidol. Further analysis of the data indicated that improvement occurred as a result of learning not to respond inappropriately, but also suggested the possibility of a more direct effect on learning mechanisms (Campbell et al., in press).

In a similar cohort of 40 autistic children, Campbell et al. (1978*a*) employed an innovative experimental design which compared haloperidol to placebo and also investigated the interaction of haloperidol with behavior therapy techniques. The mean optimal dose of haloperidol was 1.65 mg/day. Haloperidol was significantly superior to placebo in reducing the severity of withdrawal and stereotypy in children older than 4.5 years. Contingent reinforcement was a better facilitator of imitative speech than was haloperidol, but haloperidol and contingent reinforcement, in combination, significantly accelerated the process.

This series of studies illustrates how apparently conflicting results frequently can be resolved by rigorous experimental design.

Thioridazine

Although thioridazine is widely used in the treatment of disturbed children, there have been surprisingly few studies of its efficacy with this population. The two studies cited above, which compared thioridazine with haloperidol, tend to favor haloperidol as more effective than thioridazine (Ucer and Kreger 1969; Claghorn 1972).

Thioridazine has been more extensively studied in populations of mentally deficient children. One survey of the use of psychoactive edication in the institutionalized population indicated that 51 percent of the residents received medication in the institutionalized one of the most frequently used (Lipman 1970). Winsberg and Yepes (1978) note that there have been several uncontrolled studies which describe the usefulness of thioridazine in this population. Davis, Sprague, and Werry (1969) also found thioridazine to be beneficial for the specific symptom of stereotyped behavior in mentally retarded children.

Thiothixene and Trifluoperazine

Two other drugs which have been studied in this population, and on occasion compared with each other, are thiothixene and trifluoperazine. In an early study, Wolpert, Hagamen, and Merlis (1966) administered thiothixene to seven males, ages 7 to 14. Although it was an open, uncontrolled design, the study did focus on a diagnostically homogeneous group of children with childhood schizophrenia who had been ill for at least 2 years. (Interestingly, some of the children had had previous trials of LSD.) One child showed marked improvement, three showed moderate improvement, and three showed no improvement at doses of thiothixene ranging from .12 mg/kg to .19 mg/kg. Campbell et al. (1970) likewise investigated the effects of thiothixene in 10 children with diagnoses of childhood schizophrenia, many of whom were also mentally deficient. Doses ranged from 1 mg/day to 1–6 mg/day in a double-blind trial that followed an earlier crossover trial of chlorpromazine and trifluperidol. Thiothixene was as potent as the other drugs and had many fewer side effects. Waizer et al. (1972) reached similar conclusions in a single-blind evaluation of thiothixene in outpatient schizophrenic children using doses of 10 to 24 mg/day. They found the drug to be therapeutically useful while having a very low incidence of side effects.

Thiothixene was compared to trifluoperazine in a study not having a crossover, but in which the children were randomly allocated to the different groups and the ratings were double-blind (Wolpert, Hagamen, and Merlis 1967). There were eight children with diagnoses of childhood schizophrenia in each group. The drugs were found to be equally effective, and each had a low incidence of side effects.

Fish, Shapiro, and Campbell (1966) conducted an interesting controlled study of trifluoperazine in young "autistic-schizophrenic" children. This study tested not only the efficacy of trifluoperazine but also evaluated whether the degree of language retardation correlated with response. Language development did emerge as a key variable. Those children who had the least degree of language impairment showed the greatest improvement in an intensive nursery program without any phenothiazine medication. However, those with the greatest impairment in language development showed significant improvement with trifluoperazine when compared to controls. Trifluoperazine did not produce significant improvement in the mildly impaired group, and while each of the four speaking children in the control group improved, two of the four in the trifluoperazine group actually became worse, in that they developed central nervous system depression, lethargy, and apathy, and their speech production decreased.

Lithium

Campbell et al. (1972*b*) used a controlled, crossover design to compare the efficacy of lithium to that of chlorpromazine in 10 "severely disturbed" children, the majority of whom were diagnosed as schizophrenic. Doses of lithium ranged from 450 mg/day to 1,350 mg/day, with blood levels from 0.25 to 1.19 mEq/l. In general, lithium was not particularly useful in this population, although one child who had a dramatically positive response was described in considerable detail. His extreme, self-mutilative behavior and explosiveness virtually disappeared, as did his preoccupation with world destruction. The optimal dosage of lithium for him was 600 mg/day, which produced blood levels in the range of .59 to .76 mEq/l. Another controlled trial which investigated the usefulness of lithium in severely disturbed children was conducted by Gram and Rafaelsen (1972). Their study population consisted of 18 children, ages 8 to 22, all of whom had first displayed psychotic traits before age 5. Lithium dosage was adjusted to achieve lithium levels between 0.6 and 1.0 mEq/l. Lithium proved to be superior to placebo in this population and produced no more side effects than were seen in the placebo period. In an extremely thorough review of the literature concerning the use of lithium in children and adolescents, Youngerman and Canino (1978) describe only the two studies summarized above. Their comprehensive review uncovered a total of 211 reported cases of children and adolescents treated with lithium; they note that it is difficult to draw clear conclusions because of lack of diagnostic clarity. However, their impression was that the presence of an affective component indicated a greater likelihood of response. Of significance is the fact that gross neurological dysfunction did not appear to be a contraindication.

The studies of Sheard (1971) suggested that lithium may be of use for adults with severe impulse control disorders manifested in violent behavior. Rifkin et al. (1972) found that lithium may be of value in treating adolescents diagnosed as "emotionally unstable character disorder."

The problem of extreme aggressive behavior directed against self or others is frequently encountered in pervasively disturbed and mentally retarded children. Dostal (1972) commented on the potential usefulness of lithium in this context but emphasized that it is primarily useful when aggressiveness is linked to emotional lability. A position paper of the American Academy of Child Psychiatry suggested that this is an area worthy of further investigation (Campbell et al. 1978*b*). Of special importance in pediatric populations is the fact that lithium does not have major deleterious effects on cognition. In a placebo-controlled study comparing lithium and the effects of haloperidol on cognition, Platt et al. (1981) found that lithium caused only a negative qualitative change in performance on the Porteus Maze Test.

Miscellaneous Agents

The severity of the early-onset neuropsychiatric disorders and their relative resistance to conventional means of treatment have led investigators to try relatively unconventional approaches.

LSD (*d*-lysergic acid diethylamide) was the subject of research carried out in the 1960s. Abramson (1967) reviewed the use of LSD in both neurotic and severely disturbed children. The principal effect described in the severely disturbed group appeared to be a heightening of affect and arousal. Increased eye contact and decreased self-stimulation were also reported. The author pointed out the relative lack of side effects and irreversible changes. Mogar and Aldrich (1969) subsequently reviewed the use of LSD with schizophrenic children. Interestingly, the authors note that the researchers whose work they reviewed had used LSD because "all known forms of treatment had been attempted without success." One of the most consistently reported effects was the partial, transient alleviation of mutism. Mogar and Aldrich also found that 75 percent of the 91 children they reviewed had been reported in Lauretta Bender's work. Fish et al. (1969*b*) administered methysergide, a methylated derivative of LSD, to schizophrenic children. This drug is also used in the treatment of migraine headaches, probably because of its antiserotonergic activity and potential of blood vessel constriction with norepinephrine. The children studied were 2 to 5 years of age and diagnosed as having childhood schizophrenia. Even at doses of 2 mg, 7 of the 10 children showed some toxic behavioral changes, and only 3 children showed therapeutic changes without adverse effects. At higher doses, all the children showed toxic behavioral changes, and the disorganized behavior outweighed any positive effects. Interestingly, the two mute children, who were the most mentally retarded and withdrawn, tolerated higher doses. In summary, the authors noted a "complex mixture of stimulating, disorganizing, and sedating effects." These effects were, to some extent, dose-related, and tolerance developed quickly.

Campbell et al. (1976) used a crossover, double-blind design to compare levodopa and levoamphetamine in 12 schizophrenic children, ages 3 to 6. Doses ranged from 3.5 to 42 mg/day for levoamphetamine and from 900 to 2,250 mg/day for levodopa. Global ratings showed that levodopa produced improvement in some children, but the improvements did not reach statistical significance. Levoamphetamine caused an increase of preexisting stereotypies, as well as the development of stereotypies *de novo.* This also occurred with levodopa at above optimal doses.

Campbell et al. (1972*a*) also compared triiodothyronine (T_3) and dextroamphetamine in young (ages 3 to 6) schizophrenic children. The optimal dose of T_3 ranged from 12.5 to 75 mg/day. Although no significant improvement in global ratings occurred, there was a statistically significant decrease in symptomatology, the greatest improvement being in increased production of speech and lengthened attention span. Again, amphetamine (doses 1.25 to 10 mg/day) seemed to produce more problems than benefits.

A subsequent placebo-controlled, crossover study using more rigid controls and a less heterogeneous population produced more modest results, with only a few symptoms being reduced on T_3, as compared to placebo. The children with lower IQs tended to have a more pronounced response to T_3, but individual responders could not be identified by specific parameters (Campbell et al. 1978*c*).

Abbassi, Linscheid, and Coleman (1978) investigated thyroid status in 13 autistic children between the ages of 7 and 21 years. They found the concentrations of T_3, thyroxine (T_4), and thyroid-stimulating hormone (TSH) to be within normal limits, and two children who had retarded bone ages developed symptoms of hyperthyroidism when treated with T_3. A larger study of thyroid indices also found normal values (Cohen et al. 1980).

Coleman (1974) studied uric acid production in childhood schizophrenia and attempted a crossover study of allopurinol in an 11-year-old psychotic child after discovering an elevation of uric acid. She described reduction of psychiatric symptoms during the period of allopurinol administration and return of symptoms during the posttreatment phase.

In regard to vitamin treatment, Denson (1976) described vitamin B_{12} as effective in psychotic children, but systematic, placebo-controlled studies, such as the one carried out by Greenbaum (1970) with niacinamide, failed to show any advantage of this form of treatment, as compared to placebo. Numerous anecdotal reports suggest that individual children may benefit from vitamin treatment. Rigorous studies and careful evaluation of individual children with supposed marked improvement are obviously warranted.

Side Effects

Effects on EEG and Seizure Threshold. The child with seizures presents a difficult problem. There have been several reports of chlorpromazine lowering the seizure threshold in epileptic children (Fabisch 1955; Hunt, Frank, and Krush 1956; Tarjan, Lowery, and Wright 1957), and it would therefore seem advisable to avoid its use in children with seizure disorders. Similar, but less well-documented findings have also been reported for fluphenazine (Arnold and Magin 1967) and trifluoperazine (Engelhardt, Polizos, and Margolis 1972). This increase in seizure activity does not appear so frequently with thioridazine. Oettinger and Simonds (1962) found only one child in 246 to have an increase in seizure activity, and there have been reports of decrements in seizure activity in epileptic children receiving thioridazine (Kamm and Mandel 1967; Baldwin and Kenny 1966). Thus thioridazine appears to be the safer drug to use with children who have a known seizure disorder.

A recent extensive review by Itil and Soldatos (1980) distilled a number of clinical investigations and provided much practical information. The authors noted that the usual effect of antipsychotic medications is to produce excessive, diffuse slow electroencephalographic (EEG) activity. This effect usually has no clinical importance; however, transient changes, ranging from dysrhythmic groups to spike-and-wave complexes, may be associated with epileptic seizures.

In general, aliphatic phenothiazines appear to be more epileptogenic than piperazine derivatives; drugs that are more sedative have more epileptic potential, while those with prominent extrapyramidal side effects have fewer epileptogenic properties. As might be expected, patients with a history of seizures or organic brain disease are more likely to be affected. Drug-induced EEG abnormalities are most likely to occur during the initial period of treatment, during sudden changes of dose, or after abrupt withdrawal. If a seizure occurs, or the EEG rapidly deteriorates in a patient, a thorough neurological evaluation should be conducted to rule out underlying organic contributions; a change to a less epileptogenic medication should be considered as well as prophylactic treatment with anticonvulsants.

One interesting finding has been a correlation between behavioral changes (toxicity or improvement) and more marked EEG changes (Korein 1971). A similar result was reported by Saletu et al. (1975), who found a significant correlation between the beneficial clinical effects of fluphenazine in psychotic children and evoked potential changes. Winsberg and Yepes (1978) concluded that while the study of drug-induced changes in evoked potentials may ultimately prove fruitful, the results are tentative at present.

Sedative and Cognitive Effects. The effects of neuroleptic medication on severely disturbed children may be viewed from both a pragmatic and a theoretical perspective. The most persuasive finding of investigations assessing the antipsychotic medications is the decrease in psychomotor activity which they provide (Winsberg and Yepes 1978). On the other hand, the effects of these medications on learning and school performance are of special concern in the younger age population. In summarizing a number of studies, Sprague and Werry (1974) found that neuroleptic drugs produce a deterioration of performance on simple tasks, especially if memory is involved, and increase response latency. A study that they conducted with thioridazine confirmed these findings for that medication, as did an early study of Helper, Wilcott, and Garfields (1963) dealing with chlorpromazine. Recent evidence indicates that dose-response relationships may not have been sufficiently considered in some of these early studies. For example, Campbell et al. (1982) found that low doses of haloperidol may actually facilitate learning in autistic children. A finding of drowsiness and lethargy related to reduction in psychomotor activity is more pronounced with chlorpromazine and thioridazine but has also been reported with other phenothiazines.

Miscellaneous Side Effects. The side effects associated with neuroleptic medication in children are similar to those seen in adults (for review, see Winsberg and Yepes 1978). Reported side effects include blurring of vision, dry mouth, urinary retention, constipation, irritability, depression, agranulocytosis, leukopenia, eosinophilia, liver malfunction, skin rashes, weight gain, and corneal and lens damage. Effects on the cardiovascular system are less pronounced than those seen in adults.

Extrapyramidal Symptoms, Withdrawal-Emergent Symptoms, and Tardive Dyskinesia. Tardive Dyskinesia (TD), the most serious side effect of neuroleptic medications seen in adults, was discovered only after the medications had been in widespread use for several years. Thus, there is understandable concern that the use of the medications in children may expose large numbers to a debilitating side effect. To date, this problem in children has been seen only following the withdrawal of antipsychotic medication, leading to the use of the term, "withdrawal-emergent symptoms" (Polizos et al. 1973).

The study by Polizos et al. (1973) involved 34 children aged 6 to 12, who received diagnoses of childhood schizophrenia (many of the children would probably now be diagnosed as pervasive developmental disorder). The drugs used in the cohort were fluphenazine, haloperidol, thioridazine, trifluoperazine, and thiothixene. Doses given were comparable to those used in adults, and duration of treatment ranged from 6 months for thiothixene to 14 months for fluphenazine.

The clinical effect of drug withdrawal in these children was striking; all but two suffered total clinical relapse. Forty-one percent of the children also showed the emergence of involuntary movements and ataxia from day 1 to day 15 after withdrawal. The most implicated drug was fluphenazine, and the least implicated was thioridazine, with only one of nine children treated with the latter drug developing relatively mild involuntary movements and ataxia. The anatomical distribution of the movements was different from that usually seen in adults with TD. The involuntary movements were rarely in the tongue, mouth, and jaw but were primarily located in the extremities, trunk, and head, and were choreiform in nature. Also observed were myoclonic, athetoid movements, posturing, and body- and head-rocking movements. The ataxia presented as a disturbance of balance with typical drunken gait, dysmetria, tremor on volition, impaired fine coordination, and generalized hypotonia.

Polizos et al. (1973) were unable to maintain the children in the drug-free state because of their clinical deterioration, and medication was therefore reinstituted within 2 to 5 weeks of withdrawal. The withdrawal-emergent symptoms disappeared before the medication was reinstituted in half of the children, and within 1 to 2 weeks of the reinstitution of medication in the others.

In a later study involving 47 children (Engelhardt, Polizos, and Waizer 1975), there were 141 instances of neuroleptic withdrawal. Ataxia was found to be a much more frequent symptom than it is in adults, while oral symptoms were much less frequent. The symptoms remitted within 3 months in approximately one-third of the patients. In the remaining children, medication had to be reinstituted because of clinical deterioration. The order of most offending drug to least in this study was fluphenazine, thiothixene, mesoridazine, trifluoperazine, thioridazine, and chlorpromazine.

Another study addressing this issue is that of McAndrew, Case, and Treffert (1972), who retrospectively reviewed the effects of phenothiazine withdrawal in 125 chronically medicated inpatients, ages 4 to 16. Ten of the children (ages 8 to 15) were described as having developed "tardive dyskinesia." The symptoms appeared within 3 to 10 days after drug discontinuation and persisted from 3 to 12 months. Many of these children had oral manifestations, in addition to the extremity movements described by Polizos et al. (1973). In all cases, the movements disappeared within 3 to 12 months after discontinuation of medication. In a prospective study using low doses of haloperidol in 33 autistic children, Campbell et al. (in press) reported the emergence or enhancement of movement disorders in 12 percent of the study population after 3 to 11 months of treatment. Preliminary studies have been unable to detect any neurotransmitter abnormality in the cerebrospinal fluid of children who develop these symptoms (Winsberg and Yepes 1978). There has been one report of severe, persistent dystonia occurring after haloperidol administration and persisting 5 months after drug withdrawal (Shields and Bray 1976). However, it should be noted that the 5-year-old female spontaneously developed a relatively severe movement disorder (diagnosed as Sydenham's chorea) several weeks before beginning treatment with haloperidol in doses of 0.5 mg four times a day; thus, it is not clear that haloperidol was totally responsible for the subsequent, persistent movement disorder.

Similar cases of irreversible movement disorders in children following phenothiazine administration have been reported (Winsberg and Yepes 1978), and a larger followup study involving 21 children with symptoms of tardive dyskinesia, followed for a 4-year period, indicated that the problem did not remit with time, thus suggesting a similarity to adult tardive dyskinesia (Paulson, Rizui, and Crane 1973).

While the danger of tardive dyskinesia is a persistent worry to the clinician, the development of extrapyramidal side effects creates more difficulty in day-to-day management. In general, thioridazine produces a lower incidence of these extrapyramidal symptoms (Engelhardt, Polizos, and Margolis 1972) than other antipsychotic medications, and this may account in part for its frequent use in the younger age group. However, acute dystonic reactions, and extrapyramidal, parkinsonian symptoms have been associated with virtually all antipsychotic medications (Winsberg and Yepes 1978). Haloperidol has been found to cause extrapyramidal symptoms in 53 percent of psychotic children, aged 5 to 14 years, treated for an average of 39 weeks (Engelhardt, Polizos, and Waizer 1975). A 5-year study of the use of chlorpromazine, trifluoperazine, promazine, and prochlorperazine for control of nausea and vomiting in a large metropolitan hospital revealed 20 cases in which extrapyramidal symptoms occurred (Gupta and Lovejoy 1967). The cases were almost equally divided by sex, and they ranged in age from 11 months to 14 years. However, there was a preponderance of incidents in younger children. The dosages given were less than those commonly used in psychiatic conditions—7.5 to 25 mg for chlorpromazine, for example. Symptoms occurred within 5 to 30 hours of the administration of the first dose and usually consisted of cogwheel rigidity, opisthotonus, and hyperreflexia. Ataxia, oculogyric crisis, torticollis, and dystonia also occurred, but with less frequency. The symptoms usually abated rapidly with administration of benadryl.

Summary and Conclusions

Despite methodological problems, many clinical studies and rigorous trials support a place for antipsychotic medication in the treatment of pervasively disordered children suffering from childhood psychosis and autism, with or without concomitant mental retardation. It appears that lower doses are required than in adults, and cognitive blunting presents a greater problem because of the need for this age group to be actively learning. Thioridazine and thiothixene emerge from the review as the drugs which are least associated with side effects, although haloperidol appears to be more efficacious in the amelioration of specific target symptoms.

Of great theoretical interest is the fact that the drugs do not appear to have the same specifity for psychotic ideation in children as in adult patients. Instead, they are most useful for such symptoms as hyperactivity, stereotyped behavior, aggressiveness, impulsivity, self-abusive behavior, and general social adaptation. The pharmacological evidence would seem to suggest that these severe disorders in children are not on a continuum with the adolescent-onset variety of schizophrenia, but rather represent a different type of illness, more diffuse in presentation and less responsive to the current therapeutic armamentarium. This inference is in keeping with genetic studies that suggest a differentiation between early- and late-onset psychosis (Hanson and Gottesman 1976).

These factors point to the need for greater diagnostic clarity in future studies, with emphasis placed on the response of specific target symptoms. Continuing clinical trials of newer, potentially more efficacious medications are also warranted.

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Determination of Neurochemically Important Compounds in Physiological Samples Using HPLC

by George M. Anderson and J. Gerald Young

Abstract

We review the application of high-performance liquid chromatography (HPLC), coupled with amperometric (LC-EC) and/or fluorometric detection systems, to the determination of neurochemically important compounds. Methods for the measurement of the catecholamines and indoleamines (and their precursors and metabolites) in brain, cerebrospinal fluid, blood, and urine are presented.

The growing interest in liquid chromatography as a research tool has been well documented in a number of texts (Karger, Snyder, and Horvath 1973; Brown 1973; Snyder and Kirkland 1974) and review articles (Kirkland 1971; Grushka and Kikta 1977; Karger and Giese 1978; Brown and Krstulovic 1979). In the middle and late 1960s, workers began using small diameter packing (10–50 μm) to achieve efficiencies comparable to gas chromatography. The increased efficiencies, or sharpness of peaks, resulted in the following interrelated benefits: reduced separation times, increased peak capacities, and greater resolutions. The classical methods of adsorption chromatography, liquid-liquid chromatography, and ion-exchange chromatography all saw greater use because of the basic improvement in efficiency. The terms "high-performance" (referring to the greater column efficiencies) liquid chromatography (HPLC) or "high-pressure" (reflecting the 500–5000 psi pressures usually required to pump eluents through columns containing the smaller packings) liquid chromatography are used to describe the method. Practitioners of liquid-liquid chromatography were still hindered by the inconvenience, instability, and short lifetimes of column packings prepared by physically depositing a liquid stationary phase onto a support such as silica gel. Problems of stationary-phase bleed and column instability, the lack of gradient capabilities, and the necessity of pre-equilibration of mobile phases limited the use of the technique. The development of chemically bonded stationary phases in the early 1970s solved these problems. The packings are prepared by reacting organochlorosilanes with the "surface" hydroxyls of microparticulate (5–20 μm), totally porous, silica gel. Most commonly, straight chain octyl (C_8) or octyldecyl (C_{18}) groups are attached, giving the packing a nonpolar, waxlike character. These packings are used in the reverse-phase mode—that is, with mobile phases of higher polarity than the stationary phase. It has been estimated that at present 60 to 80 percent of analytical separations are accomplished using octadecyl (ODS, C_{18}) silica with aqueous methanol or aqueous acetonitrile eluents (Horvath, Melander, and Molnar 1976). Such a reverse-phase HPLC system is very practical; prepacked columns are widely available, the columns are stable and long lived; they have high efficiency, good selectivity (separation capability), and can be used for polar and nonpolar solutes. Also, they are quick to reequili-

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brate after gradients, and inexpensive, predominantly aqueous, eluents are used. They have been found to be especially useful when making direct injections of physiological samples. Recent reviews (Karger and Giese 1978; Brown and Krstulovic 1979) discuss in detail some of these advantages of reverse-phase HPLC with regard to biochemical applications. The retention time of a compound on a reverse-phase column is determined mainly by its polarity (more polar compounds eluting more quickly) and by the amount of organic solvent (e.g., methanol) added to the aqueous solvent system. Added organic solvent tends to lower the cohesive structure or—to use the term loosely—the polarity of the water and will cause all compounds to elute more quickly. In the course of method development, it is usually necessary to separate the compound(s) to be determined from a mixture of known and unknown compounds contained in a particular sample type. Although the amount of organic solvent added will cause some relative shifting of peaks, more important in this regard are *p*H control, the type of solvent added, and buffer type and molarity. Control of *p*H is especially important as both acids and bases can be shifted to a great extent by controlling the degree of dissociation. For instance, at low *p*H (≤ 4), where most acids will be undissociated, they will be strongly retained. At higher *p*H's, the polar, dissociated species will elute much more quickly. One can often shift the retention of two peaks, relative to one another, by changing the type of organic solvent added. This is more likely to be possible if the compounds have different functional groups. This selectivity has only recently been considered on a theoretical basis, and although established solubility parameter indices give some indication of possible choices, an empirical approach is required at present.

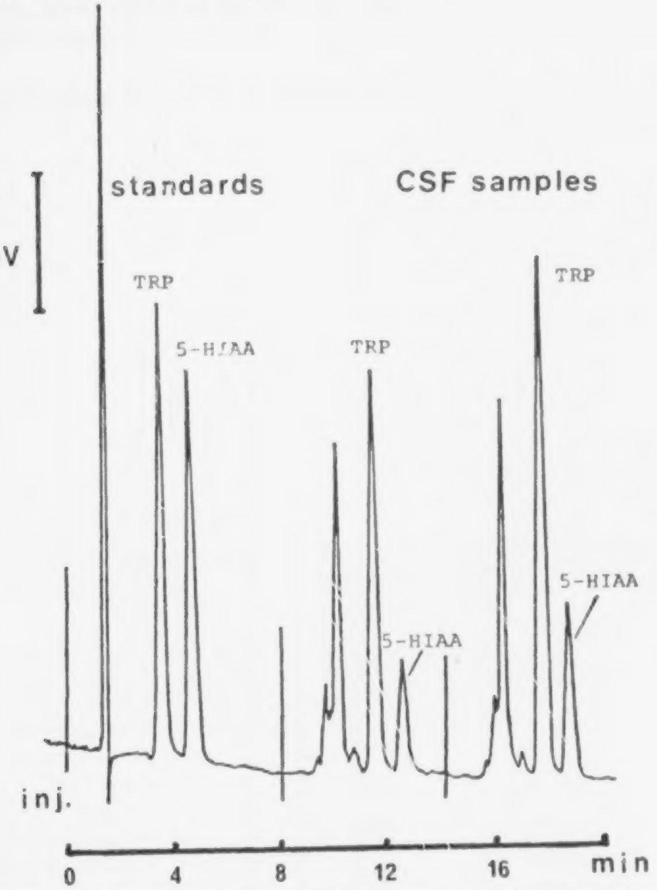
When it comes to the determination of extremely low levels of catecholamine and indoleamine neurotransmitters and their metabolites, recent improvements in detection systems may be even more important than the developments in reverse-phase HPLC. Nearly all of the HPLC determinations of neurotransmitters have employed amperometric (electrochemical) (Felice et al. 1979; Kissinger, Bruntlett, and Shoup 1979), or fluorometric (Anderson and Young 1981) detection systems. These modes of detection are very compatible with the catechols and indoles as both types of compounds are readily oxidized (and therefore detectable using amperometry) and both exhibit native fluorescence. The development of flow-through amperometric detectors for measuring compounds after their separation by liquid chromatography was, to a large degree, prompted by the need for ultra-sensitive detection of catecholamines in neurochemistry. The detectors, sensitive to 10 picograms and less of catecholamine injected into the chromatographic system, saw immediate and extensive application to the determination of catechols in brain, plasma, cerebrospinal fluid (CSF), and urine. The sensitivity of flow-through fluorometric detectors has also improved, so that detection limits, once approximately 10 nanograms for a typical indole, have been lowered to less than a nanogram; in favorable cases, to 5–20 picograms. In addition to their great sensitivities, both amperometry and fluorometry can be made extremely selective for catechols and indoles. The potential of the electrode over which the eluted compounds flow controls selectivity in the amperometric detector. This electrode, usually made of a graphite carbon paste and .1–.2 cm^2 in surface area, can be set at a low positive potential so that very few compounds in physiological samples other than catechols are oxidized and therefore detected. The limited number of compounds that are naturally fluorescent, and the ability to select the excitation and emission wavelengths, combine to allow the selective determination of catechols and, especially, indoles using fluorometry.

The basic aims of measuring the catecholamine and indoleamine neurotransmitters and metabolites in physiological samples are to correlate these measurements with other indices of central nervous system (CNS) functioning, behavioral dimensions, and specific mental disorders. Presented in the following sections are methods using HPLC (a majority using reverse-phase HPLC) coupled with amperometric and/or fluorometric detectors to determine the compounds of interest in CSF, blood, brain, and urine. Many examples have been taken from our research.

Cerebrospinal Fluid

The determination of tryptophan (TRP) and 5-hydroxyindoleacetic acid (5-HIAA) in rat CSF (figure 1) uses a commercial reverse-phase HPLC column with a 10 percent acetronitrile-90 percent aqueous

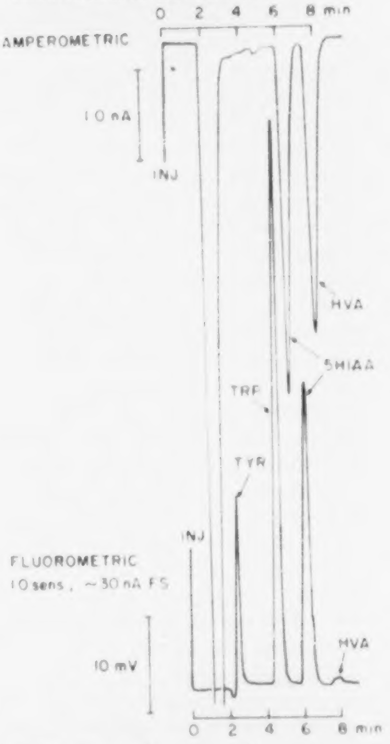
Figure 1. The HPLC-fluorometric determination of TRP and 5-HIAA in 10 μl rat CSF samples



Also shown are 1.0 ng standards of TRP and 5-HIAA. The samples contain approximately 300 ng/ml of TRP and 100 ng/ml of 5-HIAA.

buffer solvent system (Anderson and Purdy 1977, 1979). The compounds are detected fluorometrically, and the absolute detection limits of ~20 pg allow determinations to be made in rat and human CSF with only 1–20 μ1 of sample. In figure 2, tyrosine (TYR) and homovanillic acid (HVA) are determined along with TRP and 5-HIAA in a human CSF sample (Anderson, Young, and Cohen 1979). Here HVA and 5-HIAA are detected amperometrically, while TYR, TRP, and 5-HIAA are determined fluorometrically. A solvent system of 15 percent methanol allowed all four compounds to be determined in approximately 8 minutes. The solvent system *p*H was kept at 4.25, where the acids (5-HIAA and HVA) are predominantly unionized, in order to increase their retention times so that they were well separated from the TRP peak and from one another. Methanol was used instead of acetonitrile in figure 2 because the HVA and 5-HIAA co-eluted at all *p*H values (3.5–6.5) when acetronitrile was used. In both methods, CSF was directly injected into the chromatograph after simple centrifugation. Other HPLC-fluorometric (Beck, Palmskog, and Hultman 1977) and

Figure 2a. Chromatogram of standards (25 ng TYR, 5 ng TRP, 5 ng 5-HIAA, 10 ng HVA) with amperometric and fluorometric detection

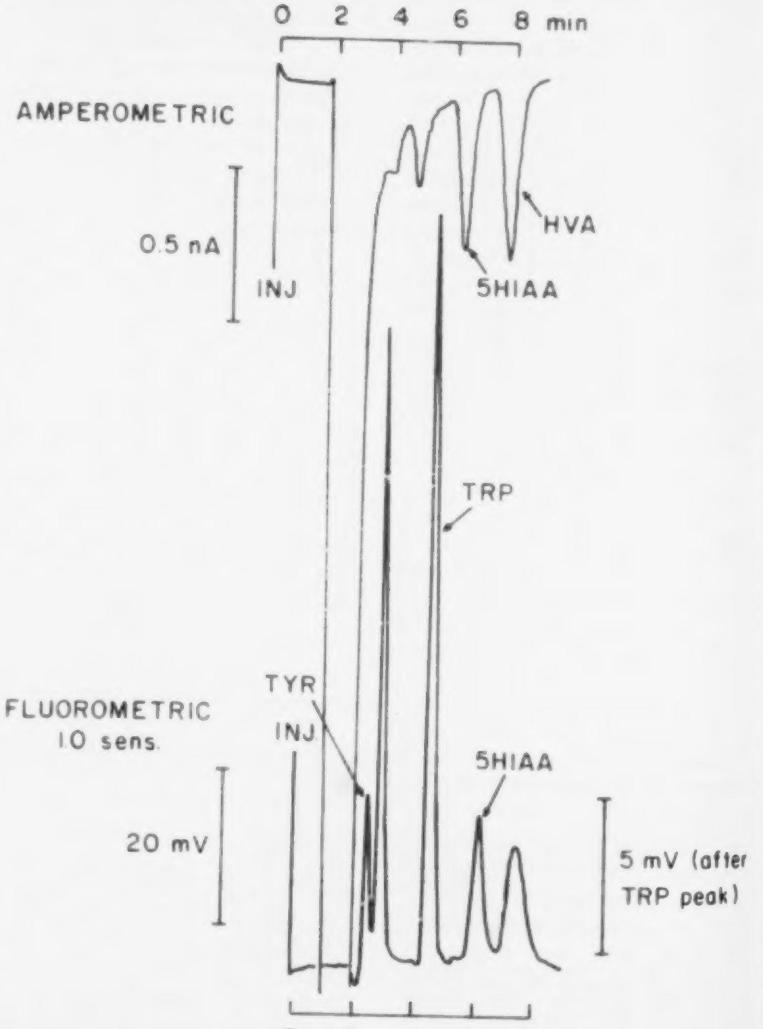


TYR is not usually separated from the amperometric solvent front.

HPLC-amperometric (Wightman et al. 1977) methods have appeared in the literature, but they require more extensive sample preparation and are limited to one or two of the compounds. The methods shown are also superior in several aspects to gas chromatographic-mass spectroscopic (GC-MS) techniques (Bertilsson et al. 1972; Åsberg et al. 1973; Fri, Wiesel, and Sedvall 1974; Swahn et al. 1976). Similarly for the determination of indoleacetic acid (IAA), the major brain metabolite of the behaviorally active trace amine, tryptamine, the CSF is merely centrifuged and then injected (figure 3) (Anderson and Purdy 1977, 1979). The compounds are detected fluorometrically with absolute detection limits of less than 10 pg. A solvent system containing 30 percent acetonitrile was employed. Indolepropionic acid (IPA) is determined along with IAA, and even though the compounds differ only in a single side-chain methylene group, they are very well separated. A *p*H of 4.0 is used in order to increase the retention of both these acidic compounds so that they are comfortably separated from the large solvent-front peak. This peak is composed of a number of merged peaks which can be separated from one another if a smaller amount of organic solvent is used, thereby increasing the retention of all the peaks; i.e., compare figure 2 (fluorometric) and figure 3. The method is much simpler, and slightly more sensitive, than the GC-MS method (Bertilsson and Palmer 1972).

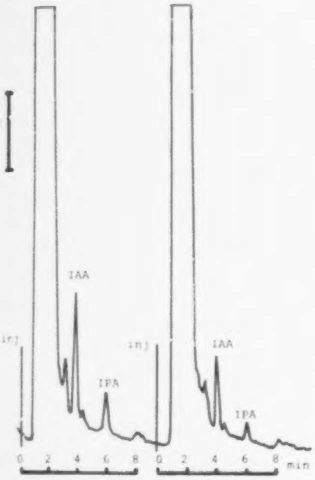
The determination of 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG), the principal central metabolite of norepinephrine, is shown in figure 4 (Anderson et al. 1981*c*). Amperometric detection was used, with an aqueous citrate-acetate buffer. A concentration detection limit of 1 ng/ml was obtained when directly injecting 40 µl of centrifuged CSF. An average value of approximately 10 ng/ml was observed in agreement with

Figure 2*b*. Chromatogram of a 20 μl, directly injected, human lumbar CSF sample



Concentrations for the sample shown are: TYR, 1.04 µg/ml; TRP, 396 ng/ml; 5-HIAA, 32.6 ng/ml; and HVA, 89.7 ng/ml. The fluorometric peaks immediately following the TYR and 5-HIAA peaks are unidentified.

Figure 3. The HPLC-fluorometric determination of IAA and IPA



Determination made in two different rat CSF samples by the direct injection of 50 μl of untreated CSF. The CSF contains approximately 5 ng/ml of IAA and 2 ng/ml of IPA.

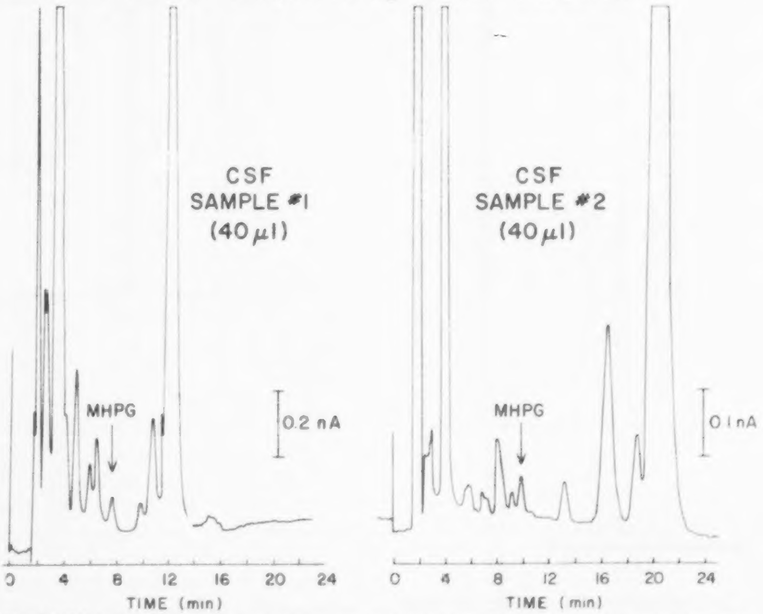
GC-MS reports. Along with many gas chromatographic, fluorometric, and GC-MS methods, one other HPLC-amperometric method has been reported. However, lengthy sample preparation and gradient chromatography was employed (Krstulovic, Bertoni-Dziedzic, and Gitlow 1980).

Blood

Samples for the determination of the catecholamines, norepinephrine (NE), epinephrine (EPI), and dopamine (DA) are prepared by purification and concentration on alumina, then injected on a cation-exchange HPLC-amperometric system (figure 5; Hjemdahl, Daleskog, and Kahan 1979). Absolute detection limits of approximately 10 pg are obtained; the compounds are quantitated by comparing the peak heights to the internal standard, a benzylamine. The method is superior to classical fluorometric techniques and compares favorably with the most sensitive radioenzymatic assays. The determination is an improvement on a previous amperometric method (Hallman et al. 1979), an adaptation of a method for determining the catecholamines in brain. Several other HPLC-amperometric methods have been reported for determining the catecholamines in plasma samples (Hansson et al. 1978; Allenmark and Hedman 1979; Freed and Asmus 1979; Fenn, Siggia, and Curran 1978), along with an HPLC-fluorometric method for NE and EPI (Yui et al. 1979).

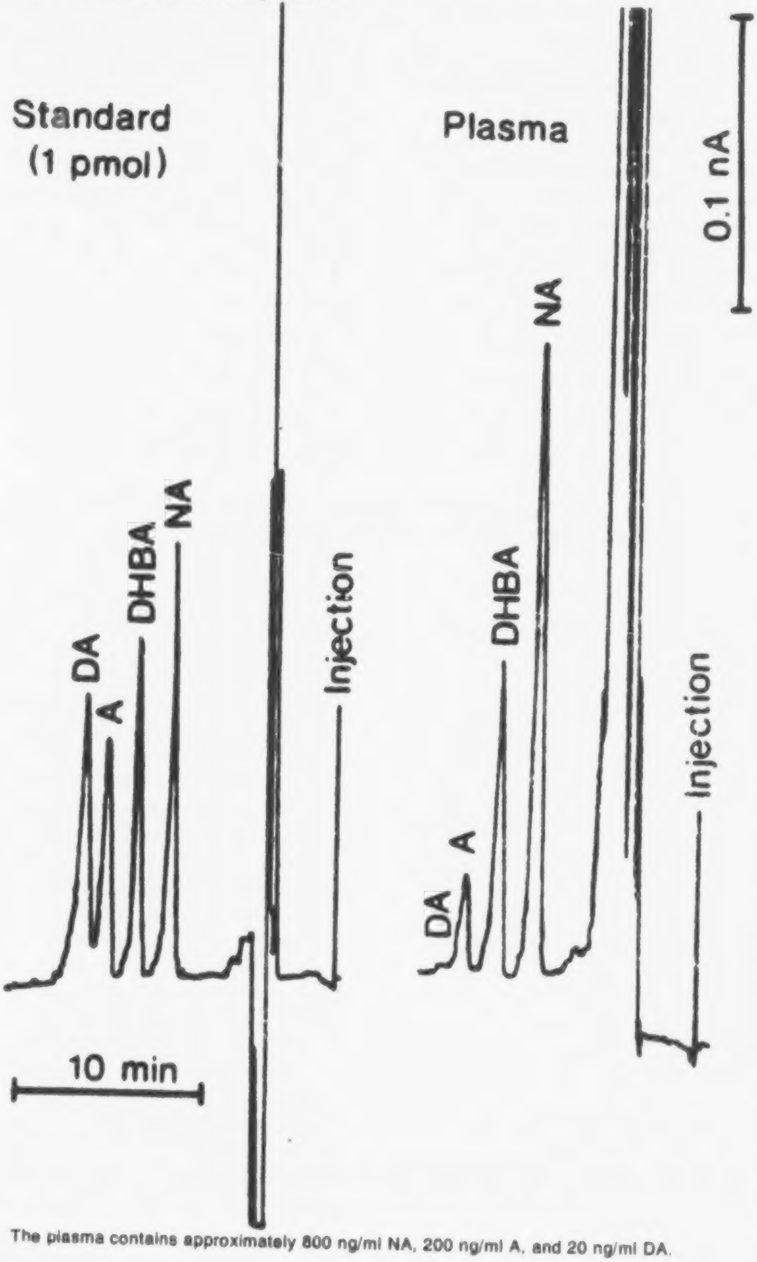
Shown in figure 6 (Anderson and Purdy 1979) is the determination of 5-hydroxytryptophan (5-HTP), the immediate precursor to 5-HT. The compound was determined, with a concentration detection limit of less than 1 ng/ml, in plasma from a patient receiving a peripheral decarboxylase inhibitor. Plasma is deproteinized by adding trichloroacetic acid, centrifuged, and the supernatant directly injected into the HPLC-fluorometric system. An aqueous solvent system containing 3 percent methanol is used. Another HPLC method for 5-HTP in plasma (Engback and Magnussen 1978) uses a postcolumn reaction, followed by fluorometric detection, and gives a detection limit of approximately 10 ng/ml.

Figure 4. HPLC-amperometric determination of MHPG in two different human CSF samples using different C_{18} columns



The MHPG levels for the samples shown are 6.7 ng/μl (sample #1) and 10.5 ng/ml (sample #2).

Figure 5. Chromatograms of catecholamine standards, norepinephrine (NA), epinephrine (A), dopamine (DA), and the internal standard, dihydroxybenzylamine (DHBA), and an alumina extract of human plasma



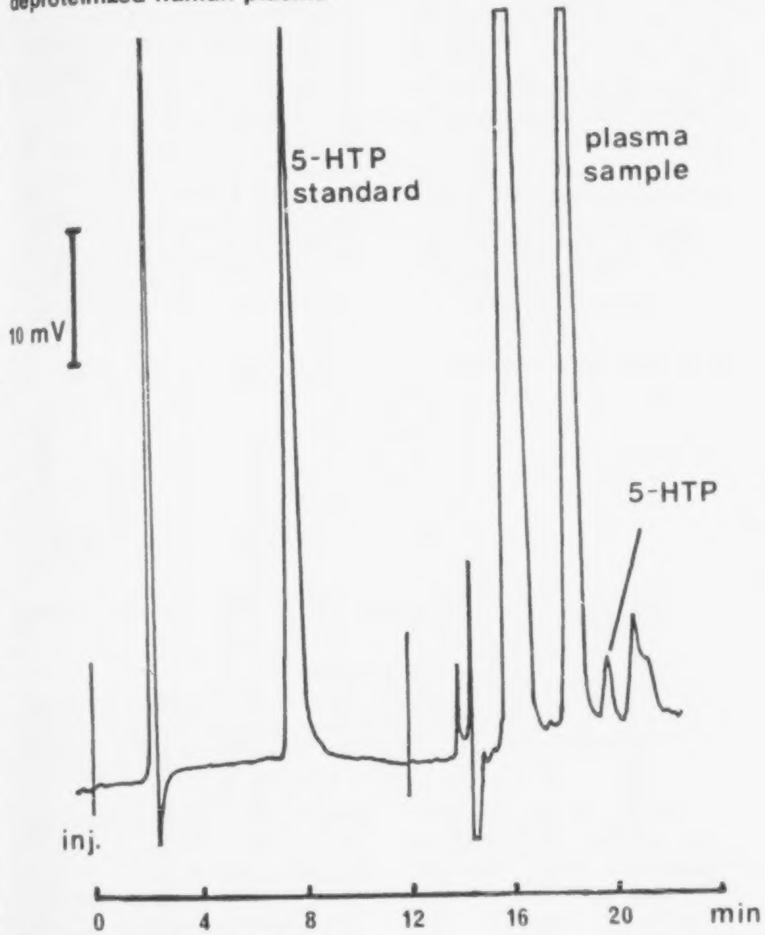
The plasma contains approximately 800 ng/ml NA, 200 ng/ml A, and 20 ng/ml DA.

For the simultaneous determination of TRP and 5-HT (figure 7, Anderson et al. 1981*b*), the whole blood or plasma samples are prepared by adding ascorbic acid and perchloric acid. The compounds are chromatographed on a reverse-phase column with a 5 percent methanol solvent system and are detected fluorometrically. Here a low *p*H (4.0) is used to shift the small 5-HT peak in front of the larger TRP peak to avoid interference from the tail of the TRP peak. Several other HPLC methods with amperometric (Sasa et al. 1978; Koch and Kissinger 1980*a*), fluorometric (Krstulovic et al. 1977; Davies et al. 1978), and spectrophotometric (Riley et al. 1979) detection are available for determining one or another of the compounds in plasma, yet none is as simple or as rapid as the method shown.

Brain

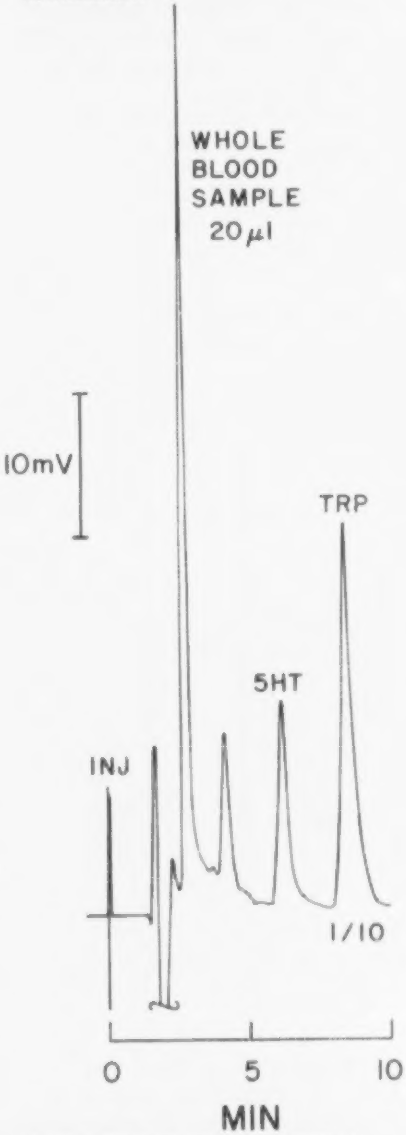
One of the first applications of HPLC-amperometry was to the determination of catecholamines in brain tissue (Refshauge et al. 1974). Since that time, many more HPLC-amperometric methods have been published (Keller et al. 1976; Sasa and Blank 1977, 1979; Fuller and Perry 1977*b*; Mefford et al. 1977; Felice, Felice, and Kissinger 1978; Hefti 1979; Loullis, Felten, and Shea 1979; Wagner, Palfreyman, and Zraika 1979; Maruyama, Oshima, and Nakajima 1980; Mefford, Gilberg, and Barchas 1980). For the determination of NE and DA in rat hypothalamus, a citrate-phosphate buffer containing an ion-pairing reagent is used to elute the compounds from a reverse-phase column (figure 8; Felice, Felice, and

Figure 6. Chromatogram of a 1.0 ng 5-HTP standard and 25 μl of deproteinized human plasma



The plasma contains 3.3 ng/ml of 5-HTP.

Figure 7. Determination of 5-HT and TRP in human whole blood after simple deproteinization

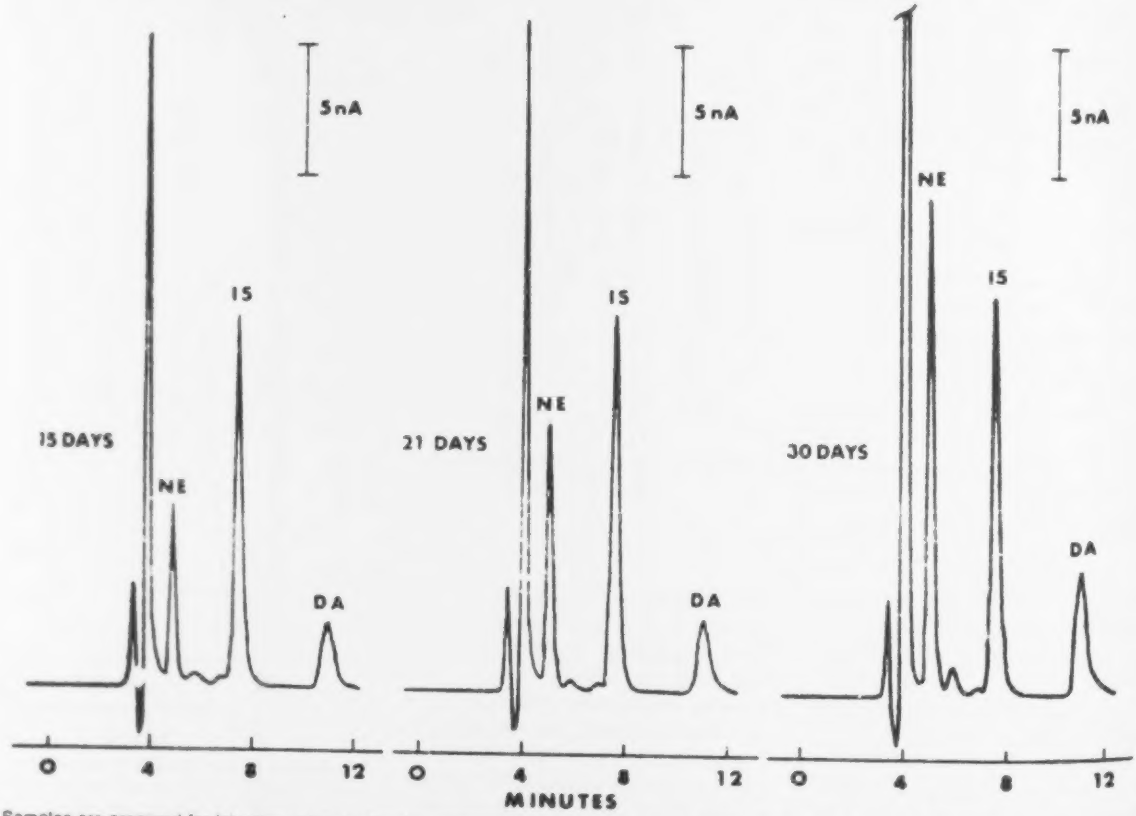


The compounds are detected fluorometrically; the concentrations in the sample shown are: 5-HT, 220 ng/ml, and TRP, 11,000 ng/ml.

Kissinger 1978). The samples are prepared, in a manner similar to that used to prepare plasma samples for catecholamine analysis, by purifying and concentrating using an alumina extraction.

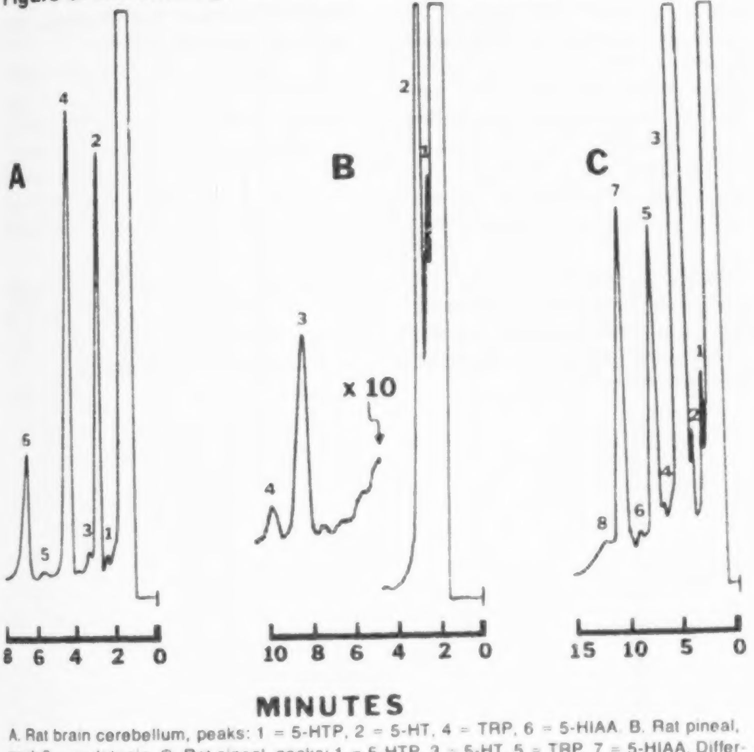
There have also been several HPLC methods developed for the determination of serotonin and its metabolites in brain. Amperometric (Sasa and Blank 1977, 1979; Loullis, Felten, and Shea 1979; Ponzio and Jonsson 1979; Koch and Kissinger 1980*b*; Lyness, Friedle, and Moore 1980; Mefford and Barchas 1980), fluorometric (Meek and Neckers 1975; Meek 1976; Neckers and Meek 1976; Fuller and Perry 1977*a*; Krstulovic and Powell 1979) and combined amperometric/fluorometric (Anderson et al. 1981*a*) detection systems have been employed. The determination of a wide range of serotonin-related compounds is shown in figure 9 (Mefford and Barchas 1980). Brain and pineal tissue were merely homogenized and centrifuged before injection into a reverse-phase HPLC-amperometric system. Normal levels of TRP, 5-HT, and 5-HIAA are easily measured in rat brain and pineal. Melatonin, an important compound present at very low levels (~1 ng per gland), also can be determined in a single rat pineal. A similar determination (figure 10; Anderson et al. 1981*a*) uses both amperometric and fluorometric detectors, and HVA is determined in addition to serotonin-related compounds. The simultaneous determination of the compounds gives an excellent check of identity and guards against possible interference in a particular sample going unrecognized. The assay of IAA and IPA in rat brain (Anderson and Purdy 1979) requires only simple sample preparation involving homogenization, protein precipitation, and centrifugation. Injection of the supernatant (50 μl—equivalent to approximately 10 mg of brain) onto a reverse-phase column eluted with a 30 percent acetonitrile solvent system gives, with fluorometric detection, the chromatogram shown in figure 11. The analytical system is identical to that used for determining

Figure 8. Chromatograms of catecholamines, norepinephrine (NE) and dopamine (DA), determined in rat hypothalmus at different ages



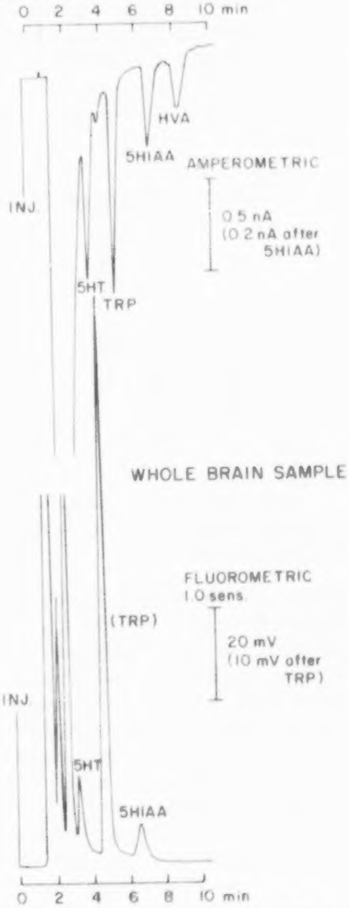
Samples are prepared for injection using an alumina extraction; dihydroxybenzylamine (IS) is used as an internal standard.

Figure 9. Chromatograms from tissue supernatants



A. Rat brain cerebellum, peaks: 1 = 5-HTP, 2 = 5-HT, 4 = TRP, 6 = 5-HIAA. B. Rat pineal, peak 3 = melatonin. C. Rat pineal, peaks: 1 = 5-HTP, 3 = 5-HT, 5 = TRP, 7 = 5-HIAA. Different solvent systems are used for each chromatogram; the same compound elutes most rapidly in B, and most slowly in C.

Figure 10. The determination of 5-HT, TRP, 5-HIAA, and HVA in whole rat brain using amperometric (downward peaks) and fluorometric detection



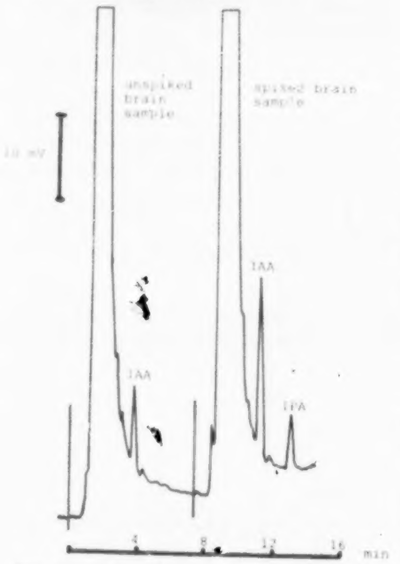
Twenty µl of a 5/1 v/w homogenate was injected.

the compounds in CSF (see figure 3). The determination of IAA in brain had only been accomplished previously using a more difficult GC-MS method (Bertilsson and Palmer 1972). Levels of 5–10 ng IAA per gram of wet weight brain are observed.

Urine

The determination of the catecholamines (Kissinger et al. 1975; Kabara, Riggin, and Kissinger 1976; Riggin and Kissinger 1977; Moyer et al. 1979; Hansson et al. 1979; Hoeldtke and Stetson 1980) and a variety of related metabolites (Felice and Kissinger 1976, 1977; Felice, Bruntlett, and Kissinger 1977; Molnar and Horvath 1977; Shoup and Kissinger 1977; Borchardt, Hegazi, and Schowen 1978; Mitchell and Coscia 1978; Hansson et al. 1979; Morrisey and Shihabi 1979; Hoeldtke and Stetson 1980; Shihabi and Scaro 1980) in urine has been accomplished using HPLC-amperometric systems. The methods require extensive samples pretreatment, but most allow simultaneous determination of several compounds. For the determination of the catecholamines, NE, DA, and EPI, in a human urine sample (figure 12; Riggin and Kissinger 1977), the sample is purified and concentrated by chromatographing on a small dis-

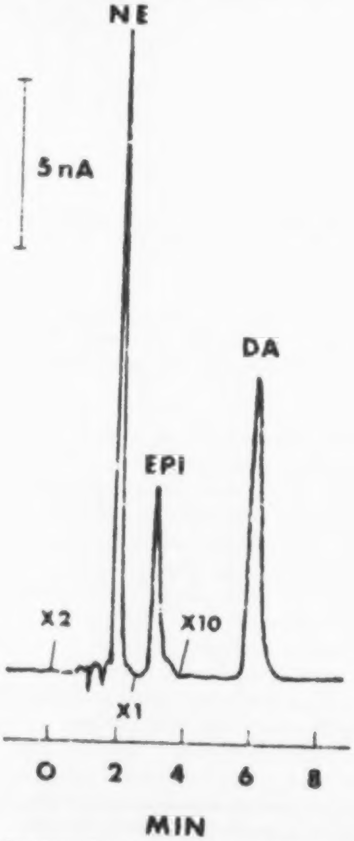
Figure 11. Determination of IAA and IPA in rat brain by the injection of a centrifuged 5/1 v/w homogenate



The spiked sample (on right) has 10 ng/g of IAA and IPA added.

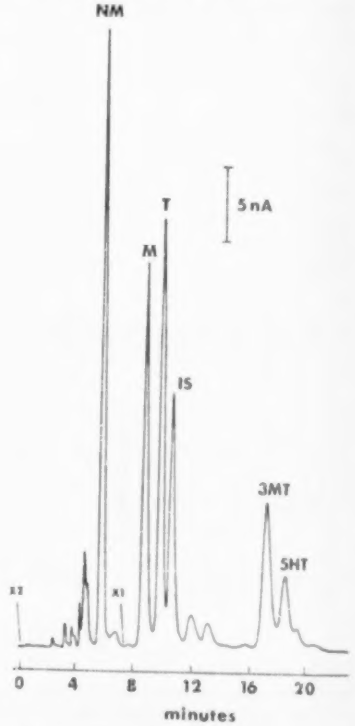
posable ion-exchange column, followed by alumina extraction. A reverse-phase HPLC column is used for the final analytical separation, and an internal standard (not shown) is usually employed. The assay of serotonin and a number of basic compounds related to the catecholamines uses a sample preparation consisting of chromatography on a small ion-exchange column and a liquid/liquid extraction (figure 13; Shoup and Kissinger 1977). Reverse phase HPLC and amperometric detection, as in the previous method, allow the simultaneous analysis of a group of important compounds. Similar methods have been reported for some of the acidic catecholamine metabolites in urine (Felice and Kissinger 1976, 1977; Felice, Bruntlett, and Kissinger 1977; Molnar and Horvath 1977; Morrisey and Shihabi 1979; Soldin and Hill 1980). Relatively few methods for measuring the catecholamines and their metabolites in urine using HPLC-fluorometric systems have been reported (Davies et al. 1978; Mell, Dasler, and Gustafson 1978; Mell 1979; Anderson et al. 1981*d*; Jackman 1981), perhaps due to a perceived need to derivatize the compounds in order to enhance detectability. When one considers the highly fluorescent nature of the indoles, there also has been little application of HPLC-fluorometric systems to the analysis of indoleamines and their metabolites in urine (Graffeo and Karger 1976; Beck, Palmskog, and Hultman 1977;

Figure 12. Chromatogram of the catecholamines isolated from human urine by ion exchange followed by adsorption on alumina



Concentrations in the urine are: NE, 60 ng/ml; E, 22 ng/ml; and DA, 510 ng/ml.

Figure 13. Chromatogram of catecholamine metabolites in normal human urine



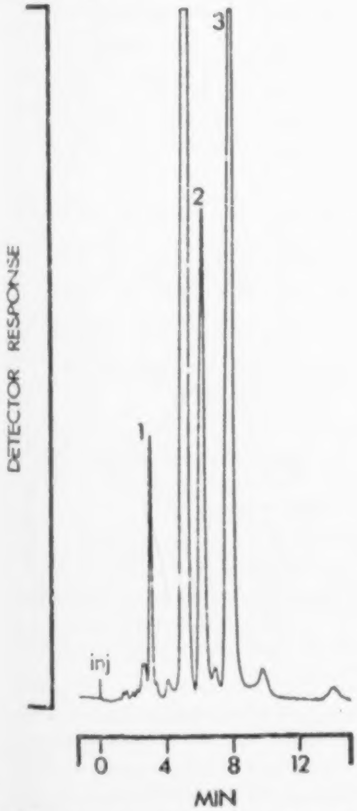
The compounds, normetanephrine (NM, 320 ng/ml), metanephrine (M, 170 ng/ml), and 3-methyoxytyramine (3-MT, 160 ng/ml) are quantitated. Also seen are peaks from tyramine (T), serotonin (5-HT), and the internal standard (IS—3-methoxy-4-hydroxybenzylamine).

Molnar and Horvath 1977; Davies et al. 1978; Anderson and Purdy 1979). In figure 14 (Beck, Palmskog, and Hultman 1977), the determination of IAA and 5-HIAA in urine is shown. An acidic urine extract is injected onto a reverse-phase column; an internal standard of 5-hydroxyindolepropionic (5-IPA) was used. Shown in figure 15 (Anderson and Purdy 1979) is the determination of TRP, IAA, and indoxylsulfate in 1 μl of untreated urine. The compounds are all easily detected by injecting urine directly because of the great sensitivity of the fluorometric detector. The identities of the peaks were checked very carefully because of the large number of peaks observed.

Conclusion

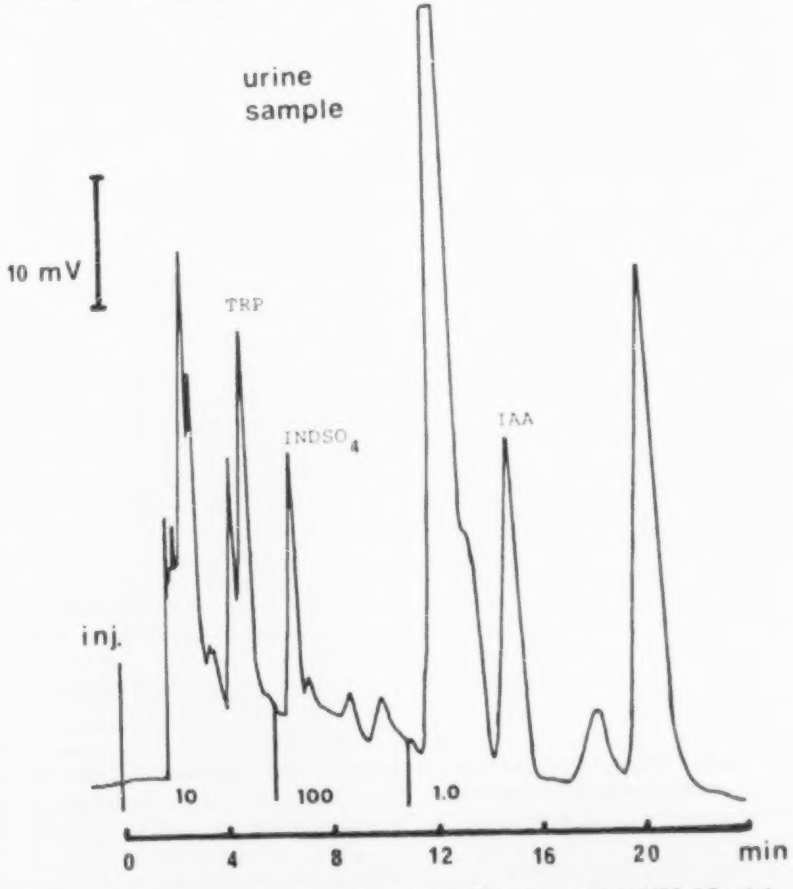
We believe this review, among others (Anderson and Young 1981; Kissinger, Bruntlett, and Shoup 1981), and the methods chosen for illustration, demonstrate the very extensive application of HPLC, coupled with amperometric or fluorometric detection, to the field of neurochemistry. The tremen-

Figure 14. Chromatogram of an acid urine extract separated on a reverse-phase column and detected fluorometrically



The compounds determined are 5-HIAA (1), 5-HIPA (the internal standard) (2), and IAA (3).

Figure 15. Chromatogram of 1 μl of untreated urine with fluorometric detection



Concentrations for the sample are: TRP, 32 μg/ml; $INDSO_4$, 120 μg/ml, and IAA, 1.8 μg/ml.

dous growth in methods is due to the sensitivity, selectivity (or specificity), and simplicity they can achieve. The sensitivities are often several orders of magnitude better than obtained with previous methods, and compare favorably with detection limits obtained using GC-MS and radioenzymatic methods—detection limits usually being in the low picogram range. The specificity is generated from the selective nature of the detection systems coupled with the great separation capabilities of HPLC. The simplicity of the methods is slightly deceptive, for although sample preparation is usually minimal and chromatographic analysis rapid, the analytical systems can be difficult to operate on a routine basis without previous familiarization. The application of HPLC methods in neurochemistry will no doubt continue at an even greater pace over the next decade.

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Attentional and Perceptual Measures: Developmental Changes

by Diane F. Harcherik, Claudia M. Carbonari, and Donald J. Cohen

Abstract

A battery of 37 tasks was assembled for neuropsychiatric assessment of cognitive functioning, motor control, perceptual abilities, vigilance, and neuromaturational status. In order to determine developmental changes within a normal population, a test battery was administered to 90 middle-class grade school children (50 boys and 40 girls), who ranged in age from 4 to 14. Statistical assessment of left- and right-handed differences produced only one significant finding, which was probably due to environmental adaptation. The only clear sex difference indicated a gross motor advantage for boys walking backward on the balance beam. All 37 tests correlated with age—with true value correlations ranging from .39 to .87.

Children with various types of neurological, psychiatric, and behavioral difficulties have trouble with fine and gross motor coordination, attending to tasks, and processing information (Graham and Rutter 1968; Cohen 1976; Rutter 1977). In the investigation of certain childhood disorders—the attention deficit syndromes and learning disabilities—the study of motor and cognitive competencies has assumed special importance because of the concept that they may reflect the underlying psychobiological substrate for the behavioral syndrome (Shaywitz 1982). For all children, the measurement of behavioral competence may help define a treatment strategy and provide a means of assessment of change. Numerous laboratory procedures, standardized tests, and batteries of measures have been described (Knobloch and Pasamanick 1962; Bialer, Doll, and Winsberg 1974; Kalverboer 1975; Peters, Romine, and Dykman 1975). However, no single test or battery has achieved broad recognition, nor has the clinical usefulness or relevance of such measures been clearly revealed. A clinician may carefully assess a child's fine motor control, sequential movements, and ability to stand still as part of the diagnostic process. But what does the clinician then do with this information? How should it be interpreted? Do the measures reveal an underlying cognitive or maturational factor? Are measures so highly interrelated that for most purposes they are redundant? How do they relate to historical and observational data and to clinical response to intervention? To approach these questions, a battery of 37 tasks was assembled to span the following areas of neuropsychiatric assessment: cognitive functioning, motor control, perceptual abilities, vigilance, and neuromaturational status. The battery contained standardized tests, tests often used by clinicians, and newly devised measures of specific skills; the battery was designed to complement the data generated by clinical assessment, historical reconstruction, and the Yale Neuropsychiatric Assessment Scales (Shaywitz 1982). This report describes the test battery and interrelations among measures. A companion report describes its clinical validity (Harcherik et al. 1982).

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Overview of the Battery

Fine motor abilities were measured by the child's ability to manipulate small objects and execute small, skilled actions; *gross motor* skills were measured by coordination in movement through space; and *perceptual motor* skills were assessed by the child's ability to attend, and motorically respond, to a changing physical target.

Vigilance was measured by the child's ability to persist in completing a task, as well as by skill in the continuous performance of the task. *Neuromaturational* level was measured by clinical tests frequently used to define nonlocalizing, "soft" neurological signs (Shaywitz 1982). *Cognitive* measures were four subtests of the Wechsler Intelligence Scale for Children (WISC-R), which assesses verbal and performance competence: block design, mazes, coding, and similarities. Children's behavior during the testing was scored using a validated rating scale that has questions in five domains (activity, attention, sociability, zestfulness, mood, and verbal expressiveness) (Dibble and Cohen 1974; Cohen, Dibble, and Grawe 1977). (See table 1 for a list of tasks.)

Population

To determine developmental changes within a normal population of school children, we used the test battery with a group of 90 middle-class grade school children (50 boys, 40 girls), who ranged in age from 4 to 14 years (mean = 8 years, 3 months). All the children were in the correct grade for their age; were functioning at grade level by teacher assessment, and, for the older grades, by standardized achievement tests; were thought to be emotionally and behaviorally normal by teachers, parents, and tester; and were physically healthy.

Procedure

Testing was performed in the children's schools in a small, quiet room to which the child was accompanied by the tester, after a brief familiarization in the classroom. During the first few minutes of the testing session, the examiner talked with the child, showed the child some of the materials, and established rapport. The tasks were introduced as games, and most looked like toys. Attention to the tasks was encouraged by praise; conversation during the testing was kept to a minimum.

For some tasks, there was an allotted length of time, and the child was encouraged to go as quickly as possible; on other tasks, children were allowed to proceed at their own pace (table 1).

Results

Subjects were divided into four age groups: 4 to 5 years, 6 to 8 years, 9 to 11 years, and 12 to 14 years. Table 2 gives the means and deviations for each task for each age group. Sample size varies among tasks because not all children completed all tasks. Some tasks involving coordination or vigilance were not completed by younger children. Also, because they were just learning to write, many of the younger children could not provide meaningful data on the alphabet-writing task.

Left-right preference was determined by which limb was used by the child for throwing, kicking, and writing. Criterion for dominance was two of the three. Seventy-five children (84 percent) were considered right-handed, and the remainder (16 percent) were left-handed. Statistical assessment of differences between left- and right-handed children (t test) produced only one significant difference. In one test of fine motor coordination (on a finger-tapping task), when children used their left hands, left-handed children tapped faster than right-handed children; when children used their right hands, left-handed children tapped as fast as right-handed children. This left-handed advantage probably represents the adaptation of left-handed children to a predominantly right-handed world, rather than an intrinsic difference in fine motor abilities. In analyzing data in which handedness was an issue, results were dichotomized by dominant and nondominant hand.

Only one of the tasks showed a clear sex difference: The gross motor task of walking the 4-inch balance beam backward showed an advantage for boys ($t = 2.45$, $p = .02$). Since no other tasks revealed a sex difference, data analysis combined the sexes.

The entire set of 37 tests correlated remarkably with age, with true value correlations ranging from .39 to .87, and probability of correlation occurring by chance of less than .05 (table 3).

Comment

In general, for this population of normal children, the tasks all seemed to reflect a global developmental trend between the ages of 4 and 14 years. On several tasks, the years between 6 and 8 appeared to

Table 1. Description and scoring of the subtests of the test battery

Task	Description	Scoring
Cognitive		
Alphabet	Print alphabet as quickly as possible	No. in 20 seconds
Maze	A series of 8 printed mazes in ascending order of complexity	Time to completion
Digit symbol	Complete a written symbol which corresponds with a particular sign	No. in 2 minutes
Block design	Duplicate design presented on a series of cards with red and white blocks	Time to completion
Similarities	Perceive and express in what way two objects or ideas are similar	Untimed
Fine motor		
Letter size	Average size of letters printed in alphabet	Average size
Insert pegs with dominant hand in round holes	Insert 20 round pegs into pegboard with 20 evenly spaced holes with dominant hand	Time to completion
Remove pegs with dominant hand from round holes	Remove 20 pegs with dominant hand	Same as above
Insert pegs with nondominant hand into round holes	Insert pegs into pegboard with nondominant hand	Same as above
Remove pegs with nondominant hand from round holes	Remove pegs from pegboard with nondominant hand	Same as above
Pegboard square	Four tasks; pegs are square, and holes are unordered; same as round pegboard, in and out with dominant and nondominant hands	Same as above
Tapping, dominant hand, trial 1	Number of taps with index finger of dominant hand in 10 seconds, trial 1	No. in 10 seconds
Tapping, nondominant hand, trial 1	Same as above with nondominant hand	Same as above
Tapping, dominant hand, trial 2	Same as above with dominant hand	Same as above
Tapping, nondominant hand, trial 2	Same as above with nondominant hand	Same as above
Gross motor		
Balance beam forward	Walk on 8 ft., 4 in. balance beam forward, heel to toe	Feet/second
Balance beam backward	Same as above, backward, heel to toe	Same as above
Balance beam, toe	Same as above, tiptoe	Same as above
Balance beam, heel	Same as above, heels	Same as above

Table 1. Description and scoring of the subtests of the test battery—*Continued*

Task	Description	Scoring
Perceptual-motor		
Reaction time 1	A buzzing noise randomly sounded at 2- to 5-second (intertrial) intervals; subject stops sound by pressing key, 20 trials	Mean reaction time
Reaction-distraction	Same as above with introduction of an auditory distraction (Scott Joplin's "The Entertainer")	Same as above
Reaction time 2	Same as reaction time 1	Same as above
Marble-in-hole	40 marbles—10 red, 10 yellow, 10 blue, and 10 green—placed in 1 of 5 slots according to color	Time to completion
Vigilance		
Road tracking	Motor-driven graph paper printed with (repeated) simulated road moved from top to bottom; subject traces road with pen for 2 minutes (repeated 13 times in 2 minutes)	Mean no. of times pen leaves track
Road tracking, speed 2	Same as above (repeated 16 times in 2 minutes)	Same as above
Road tracking, speed 3	Same as above (repeated 23 times in 2 minutes)	Same as above
Neurological		
Tongue out	Protrude tongue	No. of seconds to 20
Arms out, eyes closed	Arms extended in front, eyes closed	Same as above
Right foot, eyes closed	Stand on right foot, eyes closed	Same as above
Left foot, eyes closed	Stand on left foot, eyes closed	Same as above
Mirror turns	Rotate both arms so one hand mirrors the movement of the other, arms extended forward	Turns/second
Reverse turns	Rotate both arms so one palm faces upward and the other downward, arms extended forward	Same as above
Tap right, closed left	Tap right hand, close left hand in sequence	Sequence/second
Tap left, closed right	Tap left hand, close right	Same as above

mark a special phase of transition. This phase was noted in the letter-writing task (a plateau in letter-writing speed and size occurred around age 7) and balance beam (only three children under age 6 could walk on their heels on the 4-inch beam). For the younger children, there was an increase in reaction time from the first block of trials to the second; the younger children tired with practice and were distracted by the music introduced in the distraction trials. In contrast, older children decreased

Table 2. Mean and standard deviation for the subtests of the test battery by age group

Task	4–5	6–8	9–11	12–14	*n*	Total
Cognitive						
Alphabet	4.1±2.0	13.7±7.5	24.8±6.4	34.5±7.2	76	19.8±11.4
Maze	7.3±5.3	18.8±4.2	21.6±3.5	23.0±4.1	81	18.0±6.9
Digit symbol A	22.3±8.1	42.8±6.2	—	—	33	34.1±12.4
Digit symbol B	—	36.3±10.5	51.7±9.7	65.5±11.6	57	48.4±14.9
Block design	6.4±6.2	20.8±11.6	36.2±12.7	38.6±9.0	79	24.8±15.9
Similarities	—	14.2±4.3	20.2±3.7	24.3±2.6	43	18.4±5.4
Fine Motor						
Peg dominant in round	56.6±9.9	43.0±7.1	33.7±4.5	31.4±3.6	89	40.5±10.9
Peg dominant out round	26.2±5.3	18.1±3.7	13.8±2.4	12.1±2.4	89	17.2±5.9
Peg nondominant in round	66.5±14.5	49.2±12.3	39.4±5.4	34.4±4.4	90	46.7±14.5
Peg nondominant out round	29.9±10.8	18.4±4.2	15.0±1.9	12.9±1.4	90	18.4±7.7
Peg dominant in square	61.4±10.3	45.3±10.0	34.8±6.1	31.8±4.9	88	42.2±13.0
Peg dominant out square	24.6±5.5	15.5±2.9	11.5±2.7	10.8±2.2	88	14.9±5.1
Peg nondominant in square	72.4±13.8	50.9±8.9	40.2±5.9	33.5±4.2	88	48.1±15.6
Peg nondominant out square	24.9±5.0	16.3±3.6	13.3±2.2	11.0±2.4	88	15.9±5.5
Tapping dominant, trial 1	32.9±4.9	47.3±7.4	55.9±5.2	63.2±4.4	78	49.2±11.4
Tapping nondominant, trial 1	30.7±4.7	43.0±7.7	55.2±7.0	58.0±4.4	78	44.8±10.7
Tapping dominant, trial 2	31.8±3.4	44.5±8.5	53.5±5.1	61.3±3.1	76	47.2±11.1
Tapping nondominant, trial 2	27.0±4.6	39.1±8.4	47.6±6.6	54.6±4.9	76	41.6±11.0
Gross motor						
Balance beam forward	1.0±.5	1.2±.8	1.8±.9	1.8±.8	73	1.5±.9
Balance beam backward	.4±.1	.6±.3	1.1±.7	1.2±.5	71	.9±.6
Balance beam toe	1.3±.4	1.8±.6	2.3±.7	2.0±.5	71	2.0±.7
Balance beam heel	1.1±.4	1.5±.7	2.1±.7	2.2±.5	62	1.9±.7
Perceptual-motor						
Reaction time 1	662±130	514±156	343±88	306±40	55	451±169
Reaction-distraction	1065±487	514±148	355±85	310±40	55	506±302
Reaction time 2	822±228	478±145	324±74	286±32	55	447±208
Marble-in-hole	182±65	95±28	67±11	57±13	90	95±54
Vigilance						
Road tracking speed 1	7.3±1.1	3.2±1.9	1.8±1.3	.7±.9	56	2.9±2.3
Road tracking speed 2	7.8±1.3	4.0±1.9	2.1±1.6	.6±.6	56	3.3±2.5
Road tracking speed 3	8.1±1.1	6.9±2.0	5.1±2.3	1.9±1.8	55	5.7±2.7
Neurological						
Right foot eyes closed	4.0±2.4	8.9±6.7	15.5±6.4	18.3±3.1	77	12.3±7.4
Left foot eyes closed	2.8±1.9	9.1±5.7	16.0±5.3	17.2±4.8	78	12.2±7.0
Mirror turns	1.0±.4	1.2±.3	1.3±.4	1.5±.4	59	1.3±.4
Reverse turns	—	.9±.2	1.1±.3	1.2±.3	39	1.1±.3
Tap right closed left	.7±.2	1.0±.3	1.1±.3	1.6±.6	66	1.2±.5
Tap left closed right	.6±.2	1.1±.3	1.3±.5	1.6±.5	64	1.6±.5

Table 3. Correlations with age for subtests of the test battery

Task	Correlations
Cognitive	
Alphabet	.87
Maze	.67
Digit symbol A	.83
Digit symbol B	.71
Block design	.77
Similarities	.77
Fine motor	
Letter size	−.55
Pegboard dominant hand in round	−.80
Pegboard dominant hand out round	−.79
Pegboard nondominant hand in round	−.71
Pegboard nondominant hand out round	−.66
Pegboard dominant hand in square	−.79
Pegboard dominant hand out square	−.77
Pegboard nondominant hand in square	−.80
Pegboard nondominant hand out square	−.75
Tapping, dominant hand, trial 1	.85
Tapping, nondominant hand, trial 1	.79
Tapping, dominant hand, trial 2	.84
Tapping, nondominant hand, trial 2	.79
Gross motor	
Balance beam forward	.44
Balance beam backward	.54
Balance beam toe	.43
Balance beam heel	.51
Perceptual-motor	
Reaction time 1 (before distraction)	−.72
Reaction time with distraction	−.68
Reaction time 2 (after distraction)	−.76
Marble-in-hole	−.74
Vigilance	
Road tracking, speed 1	−.74
Road tracking, speed 2	−.80
Road tracking, speed 3	−.67
Neurological	
Tongue out[1]	—
Arms out, eyes closed[1]	—
Right foot, eyes closed	.66
Left foot, eyes closed	.68
Mirror turns, both hands	.39
Reverse turns, both hands	.40
Tap right hand, close left	.64
Tap left hand, close right	.64

[1] Dichotomous variable.

their reaction time from the first to second blocks of trials and were only mildly distracted by the music; the music may have increased their responsivity in following trials. The transition between these two responses to the reaction time task occurred in the 6- to 8-year-old group.

In summary, the broad range of measures used in this study reflect an underlying maturational process, accounting for their intercorrelations and correlations with age, as well as individual differences. In the definition of diagnostic subgroups, the distinction between maturational delay and distinctive diagnostic difference depends on the profile of a child's performance, as well as on historical and theoretical considerations. The clinical validity of this battery of measures will be described in a complementary paper. However, measures such as those presented, when seen in the context of well-defined norms, provide one approach to the specification of an individual child's abilities. Taken in conjunction with other sources of information, they may help describe areas in need of ameliorative intervention and changes in functioning coincident with psychological, behavioral, and pharmacological treatment.

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Attentional and Perceptual Disturbances in Children With Tourette's Syndrome, Attention Deficit Disorder, and Epilepsy

by Diane F. Harcherik, Claudia M. Carbonari, Sally E. Shaywitz, Bennett A. Shaywitz, and Donald J. Cohen

Abstract

Perceptual, motor, and neuromaturational competence were assessed using a battery of tasks with three groups of children with diagnosed disorders of Tourette's syndrome (TS), attentional deficit with no known organic substrate (Constitutional AD), and attentional deficit disorder in children with epilepsy (E-ADD). The purpose was to determine how the three groups related to each other on these measures and to establish clinical validation of the test battery. As predicted, the control and the TS groups did much better than the ADD and seizure groups. The TS group differed from the controls on only a handful of measures, whereas the constitutional ADD and E-ADD children were far more deviant than the TS children. The E-ADD children as a group suffered difficulties in virtually every area.

A spectrum of attentional, perceptual-motor, coordination, and neuromaturational difficulties are found in children with diverse psychiatric, learning, and behavioral disorders. Because dysfunctions in basic psychological systems such as attention are hypothesized to underlie particular psychiatric disorders, children with a constellation of behavioral difficulties (impulsivity, inattention, poor concentration) have been characterized as suffering from "attention deficit disorders" (Alpert et al. 1981). A similar constellation can be found in children with severe, pervasive developmental disturbances such as autism, as well as in normal children who are responding to temporary situational or developmental upsets and in younger children. Recent clinical and epidemiological studies of children with Tourette's syndrome (Cohen et al. 1980; Jagger et al. 1982) have suggested that a large percentage have attentional and learning difficulties which may interfere with academic achievement. Finally, children with disorders involving the integrity of central nervous system (CNS) functioning—such as epilepsy—have an increased frequency of learning and attentional problems which may, at times, be compounded by medications, such as anticonvulsants (Rutter, Graham, and Yule 1970; Rutter 1977).

In this study, we assessed perceptual, motor, and neuromaturational competence using a battery of tasks with three groups of children with diagnosed disorders: Tourette's syndrome (TS), attention deficit disorder with no known organic substrate (constitutional ADD), and attention deficit disorder in children with epilepsy (E–ADD). The purpose of the study was to compare these three groups on multiple measures that have been used clinically to assess psychological processes, as well as to provide clinical validation for this battery of measures. The tasks used have been described previously and developmental trends in normal children defined (Harcherik, Carbonari, and Cohen 1982). We hypothesized that these clinical groups and normal children would fall in a spectrum of dysfunction in the following order: normal, TS, ADD, E–ADD.

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Population

The clinical populations all received thorough psychological, psychiatric, and neurological evaluations, as described previously (Cohen 1976; Cohen et al. 1979; Shaywitz, Cohen, and Shaywitz 1979; Young et al. 1982). Diagnoses conformed to the criteria of *DSM–III* (American Psychiatric Association 1980).

The 15 children with TS (14 male, 1 female) ranged in age from 7 to 15 years (mean = 11 years) and had characteristic multiple motor and phonic symptoms with waxing and waning intensity, changing morphology, and temporary suppressibility. None of them were on medication at the time of testing. The 11 children with constitutional ADD (10 boys, 1 girl), aged 5–14 years (mean = 9.5 years), exhibited impulsivity, short attention, poor concentration, frustration intolerance, and restless overactivity. Only one ADD child was on medication, an antihistamine for treatment of eczema. The 15 children with seizure disorder (9 male, 6 female) were 4 to 13 years old (mean = 8.9 years) and had grand mal and mixed seizure disorders. Four epileptic children were on no medication, five were receiving phenobarbital, one was receiving Dilantin, and five were on a combination of drugs (generally including Dilantin and/or phenobarbital). The normal control population consisted of 90 psychologically and medically healthy school children (50 boys, 40 girls) between the ages of 4 and 14 years (mean = 8 years, 3 months), reported previously (Harcherik, Carbonari, and Cohen 1982).

Method

The test battery consisted of 37 tasks to assess functioning in the following areas: fine motor, gross motor, perceptual-motor, vigilance, neuromaturation, and cognition. Tasks consisted of frequently used clinical procedures, standardized tests (subtests from the Wechsler Intelligence Scale for Children; WISC–R), and especially designed, game-like laboratory tasks, as previously described (Harcherik, Carbonari, and Cohen 1982). The entire battery took 40 to 70 minutes to administer to the clinical groups and approximately 40 minutes for the normal children. The clinical groups were tested in a quiet room in the Yale Child Study Center. After several minutes of familiarization, children were presented with the tasks as "games" and were encouraged to "do their best." Details of the tasks and developmental patterns have been presented.

Statistical Analysis

As previously shown, performance on all tasks improved with age (Harcherik, Carbonari, and Cohen 1982). The developmental trend was also observed with clinical groups (between-groups analysis of variance by age, $p = .01$). Therefore, analysis of variance statistics were covaried by age (ANCOVA) for all tasks. If the results of the ANCOVA were significant, Scheffé's contrast procedure for corrected treatments was used to determine which contrasts were significantly different from zero or between which diagnostic groups there was a difference. Scheffé's S-method did not indicate significant differences on some of the ANCOVAs which had significant F ratios. This was due to the single range Scheffé's method used, resulting in a more robust test. In data analysis, these results were considered nonsignificant, giving further strength to the significant results achieved.

Results

As predicted, the normal and TS groups did much better on many of the tasks than the ADD and seizure-disordered children. On several tests, the TS group deviated significantly from the normal children.

Cognitive Functioning. The four WISC–R subtests provided a general profile of cognitive competence in the clinical groups and normal children. The normal children scored higher than all clinical groups on the digit symbol (B version), higher than the seizure-disordered children on the mazes and block design, and higher than both the ADD and seizures group on similarities.

Fine Motor. There were no differences among the four subgroups on the size of letters when children were asked to write the alphabet as quickly as possible. However, the normal children wrote significantly more letters than the three clinical groups in the 20-second allotted period. In the pegboard tasks, children were instructed to place either round or square pegs into randomly arranged holes; when finished, they were instructed to remove the pegs as quickly as possible. The normal children and TS patients were faster than the E–ADD children on all trials, and the normal children were also faster than the ADD children in inserting pegs in the round holes using their dominant hand. The E–ADD children were slower than all other groups in removing the pegs in all trials.

Gross Motor. The normal children and TS group walked backward on their heels faster than the E–ADD children. There were no differences among the groups in walking forward on the 4-inch balance beam. The normal children were able to place more marbles in color-coded holes than the ADD and E–ADD children; on this task, the TS children were also faster than the E–ADD children.

Perceptual-Motor Vigilance. On the road-tracking task, children were instructed to keep a felt-tipped pen in the middle of a printed roadway which moved at slow, medium, and fast speeds. On all three speeds, the E–ADD children went off the track significantly more often than any of the other groups. On the medium speed, the TS and ADD children also veered off the track more often than the normal children.

Neuromaturational Measures. The TS children were able to hold out their tongues and arms with their eyes closed for the allotted 20 seconds; in contrast, 44 percent of the ADD and 39 percent of the E–ADD children had trouble holding out their tongues, and 38 percent and 18 percent, respectively, had trouble holding out their arms with their eyes closed. The normal children were able to stand on their right feet with their eyes closed significantly longer than the ADD and E–ADD children, a further measure of the motor impersistence of these two clinical groups.

Discussion

Formal assessment of motor skills, cognitive performance, and neuromaturation are standard aspects of the child psychiatric examination. Individual differences, and unusual profiles of competence and dysfunction, are essential to the understanding of a particular child's disorder. In this report, however, we focus only on group differences, as a way of approaching the clinical validity of this battery of measures and major differences among three groups of clinical disorders in which attentional and motor difficulties are prominent features. Based on this study, there is a spectrum of attentional, motor, and neuromaturational difficulty in which, as a group, TS children are closest to normal, and children with definite CNS dysfunction (epilepsy) and behavioral signs of ADD are most deviant.

While clinical assessment and epidemiological evidence suggest that, as a population, TS patients have a high percentage of attentional and learning difficulties, on this battery they differed from normal children on only a handful of measures. For example, they did not adapt so quickly as normal children to changes in speed of the road-tracking task, and their coding (digit symbol B) was significantly impaired. It is our impression that TS children, as a group, can perform at a much improved level on tasks such as the ones we have employed, when the situation is highly structured and distractions are minimized. In the classroom or when alone at home doing homework, behavior deteriorates, as the children's attention drifts and they are more preoccupied with either the suppression (in school) or expression (at home) of motor and phonic symptoms. The clinically frequent symptomatic difficulty with writing was observed in this study as well: TS patients wrote fewer letters than normal children in the short time allotted. The TS children in this study were not so severely impaired as some whom we have studied in other projects. The results indicate that, with sufficient structure, TS patients can be expected to perform well as a group.

The children with constitutional ADD and ADD associated with epilepsy were far more deviant than the TS children, as would be expected from the selection criteria. The ADD and E–ADD children all satisfied criteria for attentional disturbances, and many had clinical findings of nonlocalizing motor dysfunction; only a subgroup of the TS patients satisfied the criteria for ADD. Most impressive, the E–ADD children as a group suffered from difficulties in virtually every area investigated. The multiple tasks revealed the difficulties which the epileptic children experience in organizing their motor performance and in cognitive tasks. The degree to which these differences reflect the underlying brain dysfunction, as such, the medication (particularly phenobarbital), or a combination of factors could not be determined from this study. Careful documentation of the difficulties of the E–ADD children, however, proved of clinical value in guiding families and suggesting interventions in relation to schooling. Rigorous measurement of attentional, motor, and neuromaturational findings adds increased persuasiveness to medical recommendations in relation to school interventions; in addition, such measurement may provide useful yardsticks for assessing developmental changes, the impact of improved or worsened control, or the results of medication changes. In the clinical evaluation of children with attentional and motor performance difficulties, clinicians require simple, easy to administer tests which can provide standardized scores. The results of this study, along with others using similar approaches, suggest that this is an opportune time for clinical application of behavioral measures which previously have been used extensively in clinical investigation.

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The Yale Neuropsychoeducational Assessment Scales

by Sally E. Shaywitz

Abstract

The Yale Neuropsychoeducational Assessment Scales (YNPEAS) represent a newly developed tool designed to test the hypothesis that homogeneous subgroups of children with the more subtle neuropsychiatric disorders may be discerned and classified through shared historical, behavioral, familial, anatomic, neuromaturational, and biochemical characteristics. Consisting of a series of parent, physician, and school-related integrated assessment scales, the YNPEAS provide for the creation of a broad, multidimensional data base for each child. A major innovation of the YNPEAS is the provision of a mechanism for the orderly processing of the mass of clinical information into operational statements compatible with *DSM-III* constructs. This article presents the development of each of the component parts of the YNPEAS while also providing the historical perspective necessary to better comprehend the role of each of the scales. This instrument should be useful to both researcher and clinician as a tool with which to follow the natural history of a phenomenon; relate clinical dimensions across different diagnostic subgroups; and elucidate the genetic, social, and physiological interrelationships in the emergence or continuation of a disorder.

Because all aspects of scientific investigation in pediatric neuropsychiatry depend upon reliable and valid clinical assessments, diagnostic process has, by necessity, assumed a major focus of the Yale Neuropsychiatric Investigative Group. To this end, we have developed a series of integrated scales, the Yale Neuropsychoeducational Assessment Scales (YNPEAS), that provide a mechanism for recording historical events and clinical observations in a consistent, systematic manner. In this report we will concentrate, in particular, on the use of the YNPEAS to improve the standardization and consistency of the clinical evaluation of those more subtle disorders of behavior and learning characterized in *DSM-III* (American Psychiatric Association 1980) as attention deficit and conduct disorders. These parent-, physician-, and school-related instruments are based upon and replace a series of assessment schedules that have been used at Yale and elsewhere (for review, see Orvaschel, Sholomskas, and Weissman 1980). The YNPEAS provide for the creation of a general data base for each child; information is obtained and recorded about the child's background, development, and current status. Core components include *historical* (Yale Children's Personal Data Inventory and School and Family Information Form), *examination* (Yale Stigmata Schedule and Yale Neuromaturational Examination), and *behavior rating* (Yale Behavior Rating Scale) schedules. Such a system of multidimensional scales provides the multivariate framework essential for establishing correlations between clinical dimensions and biological measures. Thus, the YNPEAS should be use-

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ful to both clinicians and researchers as a tool with which to follow the natural history of a phenomenon; relate clinical dimensions across different diagnostic subgroups; and elucidate the genetic, social, and physiological interrelationships in the emergence or continuation of a disorder.

Historical Dimension

Central to the diagnostic process is the acquisition of complete and pertinent historical information. At the Learning Disorders Unit (LDU), this information is initially represented by parent responses made on the Yale Children's Personal Data Inventory (YCPDI), a 55-page, 800-item computer indexed form encompassing demographic information, genetic background, pre- and perinatal events, developmental and social history, symptomatic survey, educational experiences and current areas of difficulty (see appendices 1 and 2). A major innovation of the YCPDI is the incorporation of questions that permit *DSM–III* criteria (American Psychiatric Association 1980) to be used in diagnosis. Information regarding specific constructs determined by operational definitions provided by *DSM-III*, such as attention, activity, impulsivity, and conduct disturbances, is represented by a series of scales consisting of questions tapping that particular area. The scales were obtained initially by surveying a population of elementary school age boys of normal intelligence grouped into those receiving special educational services because of learning difficulties and those not requiring special assistance. Of the 800 questions, 200 were found to differentiate the two populations at the $p < .05$ level of significance. From these 200 significant items, scales were constructed to reflect a particular characteristic or trait. Multiple questions were used to arrive at a specific construct, thus allowing for change in symptomatic presentation with development and also to intensify the effects of each of the questions and, therefore, the reliability of obtaining that particular construct. The use of a scale of items minimizes the effects of misinterpretation or omission of any single question. While the scales were initially developed to reflect a cognitive construct, the items on each scale were subjected to statistical scrutiny and determined to have reliability as indicated in table 1. The scales are still undergoing modification and should not be considered complete.

This systematization of information classification based on *DSM–III* criteria avoids the major obstacles to reliability and behavioral diagnosis as detailed by Spitzer and Williams (1980). Information variance is minimized by providing consistent sets of information for all patients; these data are recorded in a systematic manner to provide a diagnosis following inclusion and exclusion criteria and, therefore, are not subject to differential recording based on the examiner's recall or memory. Clearly, the use of operational diagnostic criteria should minimize operational variance in diagnosis.

Although the ultimate validity of this approach will rest heavily on the validity of *DSM–III* itself, in our study in progress, initial use of the YCPDI has enabled a differentiation of learning disabled boys from nondisabled schoolchildren with an accuracy approaching 90 percent.

Physical Dimension

While there is no question of the critical importance of an in-depth textured history to the diagnostic process in children presenting with neuropsychiatric disorders, the role of the physical examination remains controversial, principally as a consequence of the inability to relate convincingly the findings on this examination to the child's behavior and learning. Clearly, all would concur that neither the general pediatric assessment nor the typical neurologic examination searching for signs of

Table 1. CPDI Scales

Scales	Reliability (overall .9052)
Conduct disturbances	.8810
Impulsivity-disinhibition	.8735
Adaptability-modulation	.9549
Activity	.9248
Fine motor acquisition	.8938
Language	.9468
Emotional sensitivity	.8422
Attention	.9143
Cognitive acquisition	.9052

asymmetry or structural damage is productive in this instance. Two areas of examination, however, have indicated a potential worthy of further clarification—the assessment for minor congenital anomalies and the neuromaturational examination.

Minor Congenital Anomalies (Yale Stigmata Schedule; appendix 3). Congenital anomalies may be indicators of aberrant prenatal development reflecting either genetically determined altered embryogenesis or an insult early in pregnancy. Characteristically, minor anomalies are of no medical or cosmetic consequence to the patient and would be overlooked on a general physical examination.

Examination of children from birth to adolescence has indicated the rarity of three or more anomalies in a child otherwise free of indicators of major system disturbance (Marden, Smith, and McDonald 1964). In contrast, Smith and Bostian (1964) noted that 42 percent of children with idiopathic mental retardation demonstrated at least three of these minor anatomic defects. These authors suggested, therefore, that the presence of a high number of associated anomalies was indirect evidence of a significant impairment in embryonic development that not only influenced the occurrence of the anomaly, but was also associated with disordered central nervous system (CNS) development. Other investigators have now used the presence of a high number of anomalies to distinguish various groups of normal and disabled children and to suggest a prenatal origin to the difficulties experienced by the high-anomaly group.

Waldrop and associates (Waldrop and Goering 1971; Waldrop and Halverson 1971), standardizing a set of minor anomalies originally used by Goldfarb and Botstein (1956), have now reported a series of investigations that indicates the stability and reliability of anomaly scores during childhood. Goldfarb and Botstein's initial observations of the presence of an increased number of anomalies in severely disturbed children have now also been confirmed by Campbell et al. (1978) and Steg and Rapoport (1975). Using this system, Quinn and Rapoport (1974) have related an increased number of anomalies to a history of both obstetric complications and paternal hyperactivity. However, later investigations (Mattes, Gittelman, and Levitt 1980), applying the same scoring system, have not been able to replicate these findings. Of particular interest has been the recurring association of high anomaly scores with difficulties of modulation of activity, impulsivity, and aggression. Waldrop et al. (1978) have found minor anatomic defects observed during the newborn period to predict difficulties with attention, aggression, and impulsivity at 3 years of age. Significant relationships have also been reported between preschool anomaly scores and hyperactivity at both 2½ (Waldrop, Pederson, and Bell 1968) and 7½ years of age (Waldrop and Halverson 1971), as well as between high anomaly scores in elementary school boys and teacher ratings of increased activity (Waldrop and Goering 1971), negative peer judgments (Halverson and Victor 1976), early onset of hyperkinesis (Quinn and Rapoport 1974), and increased dopamine-β-hydroxylase (DBH) activity (Quinn and Rapoport 1974); others (Mattes, Gittelman, and Levitt 1980), however, have not been able to confirm the finding concerning DBH. Interestingly, in girls a finding of many anomalies appears to correlate with inhibited, withdrawn, and negative behavioral characteristics (Waldrop and Goering 1971; Waldrop and Bell 1976; Burg et al. 1978). The number of anomalies does not appear to correlate with overall or Performance IQ (Waldrop, Pederson, and Bell 1968; Rosenberg and Weller 1973; Steg and Rapoport 1975)—a finding that tends to enhance the significance of the association of these defects with a diagnosis of disturbances in learning and language function (Rosenberg and Weller 1973).

In selecting the anomalies to be surveyed in the YNPEAS, our aim was to develop a scale that would enable us, and other investigators as well, to use the rich source of data based on Waldrop's system, and yet, at the same time to extend these obervations by taking note of information that might reflect more recent findings or other dimensions. For example, the Yale (Shaywitz, Cohen, and Shaywitz 1980) and University of Washington (Streissguth, Herman, and Smith 1978) groups have now described difficulties in attention, activity, and learning in children born to alcoholic mothers; and it may well be that among the subgroups of children with attention deficit disorder, there exists a cohort with a teratogenic etiology. Indeed, it is tempting to speculate that in those studies documenting an association between the presence of an increased number of anomalies and learning, attentional, or activity regulation difficulties, some of the children may have represented examples of what we have termed the expanded fetal alcohol syndrome (EFAS) (Shaywitz, Cohen, and Shaywitz 1980). Although for the most part, there is little overlap between the features of fetal alcohol syndrome (Clarren and Smith 1978) and those included in Waldrop's survey, there are some shared anomalies involving head circumference and morphologic aberrations of the eyes, ears, and mouth. An association has been noted between the Waldrop anomalies and poor verbal performance (Rosenberg and Weller 1973), and we have now reported an apparent association between language difficulties and maternal ethanolism (Shaywitz, Caparulo, and Hodgson, in press). Abnormalities of dentition have been associated with both developmental delay (Goodwin and Erickson 1973) and fetal alcohol syndrome and have been included in the Yale Stigmata Schedule (YSS). The remaining anomalies not represented on either the Waldrop scales or thought to occur in fetal alcohol syndrome were included because of an association with genetic disorders affecting academic performance (Bennett, LaVeck, and Sells 1978; Waber 1979; Shaywitz, Caparulo, and Rushton 1980) or based on the clinical experience of the investigator.

Neuromaturational Examination as an Index of Brain Function

Historical Influences. The special role afforded what we have termed the neuromaturational examination (NME) as the criterion variable in establishing a relationship between brain and behavior necessitates an awareness of the historical influences that have shaped current concepts. Reports (Meyer 1904; Bailey 1906; Goldstein 1936) dating back to the turn of the century describe a characteristic behavioral pattern in adults following brain injury. A recurrent thread of impulsivity, distractibility, low frustration tolerance, and memory difficulties highlights these observations. The pandemic of 1917 produced a new series of descriptions of behavioral disturbances, this time following encephalitis in children (Hohman 1922; Bender 1942; Greenbaum and Lurie 1948). However, perhaps the most influential and enduring support for the notion of a specific behavioral syndrome in children arising from brain damage is that provided by the work of Strauss and associates (Werner and Strauss 1941; Strauss and Lehtinen 1947). In a now classic report, Strauss and Lehtinen in 1947 formulated the conceptual entity of the "brain-injured [damaged] child." Surveying a population of mentally defective institutionalized children and using the history or neurologic examination as support for a diagnosis of brain damage, the investigators classified children into two groups: an exogenous group in whom the neurologic examination or history was thought to provide evidence for cerebral insult and an endogenous group for whom such information was lacking. Behavioral ratings provided by teachers and caretakers indicated much overlap in the cognitive and emotional styles of the groups; however, there appeared to be an excess of hyperactive, distractible, impulsive, emotionally labile, and perseverative behaviors in the exogenous or brain-damaged group. As if by sleight of hand, these vaguely defined behavioral traits based on nonvalidated indicators of brain injury were now, in and of themselves, to be considered as indicators of brain injury or damage. Often forgetting or unaware of the tenuous foundation that served as the rationale for diagnosing brain damage, investigators embraced the concept of the brain-damaged child both as a research tool and a diagnostic category. The notion of Strauss and Lehtinen (1947, p. 20) that "all brain lesions, wherever localized, are followed by a similar kind of disordered behavior" has been criticized on many levels and is no longer considered tenable. The validity of the concept of brain damage is itself in question because it has never been established that children designated as brain damaged on the basis of the behavioral pattern described by Strauss and Lehtinen have sustained CNS damage. Furthermore, in cases with documented (anatomic) cerebral insults, not all children exhibit those abnormalities of behavior supposedly diagnostic of brain damage. Even in cases in which brain damage is assumed and there is a behavioral disturbance, the nature of the association remains problematic. Instead of being causal in nature, the apparent relationship may be coincidental (Pond 1961) or a result of CNS injury causing impaired cognitive function which in turn leads to a secondary behavioral disturbance (Rutter, Graham, and Yule 1970). Others have postulated altered environmental reactions to the limitations produced by structural damage to the nervous system which in turn provokes abnormal behaviors (Knobloch and Pasamanick 1962; Gallagher 1957; Sameroff and Chandler 1975). In this view, the catenation of developmental events originating with constitutional defect leading to behavioral deviation as the inevitable outcome is discarded in favor of a more dynamic, transactional model acknowledging the bidirectionality of the effect of cerebral insult on both the child and his environment.

The concept of the brain-injured child soon evolved into that of minimal brain damage, a term with multiple meanings, sometimes referring to the behavioral syndrome described by Strauss and, in other instances, held to be indicative of certain cognitive traits, motor atypicalities, or a combination of behavioral, cognitive, and motor disturbances. Vaughn (1963), reflecting the prevailing view of the centrality of minor neurologic abnormalities to the concept of brain damage, offered the following description:

> Conditions in which there is very little or no specific abnormality or neurologic sign . . . have a number or all of the following minor abnormalities of tone, poor motor coordination, restlessness, partial learning difficulties.

Many articles appeared in the late 1950s and early 1960s describing various aspects of this syndrome with much attention focused on the neurological correlates. In 1962, the Oxford International Study Group on Child Neurology (Bax and MacKeith 1963) recommended that the term "minimal brain damage" be discarded and replaced by "minimal brain dysfunction." A further recommendation was that increased consideration be given to classifying this heterogeneous group of children into more homogeneous subgroups; possibilities suggested focusing on the neurologic dimensions—"choreiform syndrome" (Prechtl and Stemmer 1962) and "developmental clumsiness" (Gubbay et al. 1965)—or on the behavioral construct—"hyperkinetic syndrome" (Laufer and Denhoff 1957).

The many facets of the more subtle neurobehavioral disorders (attention deficit disorders, conduct disorders) and the presumed interrelationship of their components (e.g., indicators of minor neurologic dysfunction to behavioral abnormalities) continue to attract and confuse investigators, reflecting a lack of both well-defined, reliable, consistently applied sets of behaviors and neurologic aberrations. What we have witnessed in the past four decades has been the use of a poorly defined set of behavioral traits to correlate with an equally poorly defined and ever-changing array of minor neurologic abnormalities. Provision of inclusion and exclusion criteria in the *DSM-III* diagnostic categories of attention and conduct disorders, particularly, offers a beginning step toward establishing operational definitions for the behavioral side of the equation. While a number of studies (Bialer, Doll, and Winsberg 1974; Peters, Romine, and Dykman 1975; Touwen 1979) provide criteria for the diagnosis of minor neurologic abnormalities, the same finding, e.g., choreiform movements, may be assessed differently by individual investigators, and there has been no uniform core of minor neurologic abnormalities used across studies. Perhaps an even more cogent question relates to the significance of the neurologic examination in children with subtle neurologic disorders. This issue has been examined from several different viewpoints; in one approach children with CNS injury as defined by cerebral palsy, head injuries, or epilepsy (Harrington and Letemendia 1958; Graham and Rutter 1968; Eisenberg 1957; Rutter 1977) were evaluated for behavioral disorders; an alternate method targeted children with diagnosed behavior and/or learning problems who were then examined for indicators of minor neurologic dysfunction (Adams, Kocsis, and Estes 1974; Shaffer, McNamara, and Pincus 1974; McMahon and Greenberg 1977). Irrespective of the strategy employed, there has been no definite correlation observed between neurologic dysfunction and behavior/learning abnormality but rather an inconsistent relationship that has shown a significant association with other factors such as socioeconomic status, intelligence, sex, and family situation. What emerges is a lack of a direct one-to-one, input-output relationship between performance on a neuromaturational examination and behavioral status. A cautionary note has been sounded by Kalverboer (1975), who used the techniques of quantitative ethology in a study of children of preschool age. While neurologic status at 5 years accounted for only a small amount (4–8 percent) of the variance in behavior, sex and environmental factors were found to be significant determinants of the child's behavior patterns.

Measures of Neuromaturational Function. The choreiform syndrome, representing an example of the transformation of a neurologic finding to form the basis of a behavioral entity, also embodies the controversy surrounding the significance of minor neurologic abnormalities. First noted as muscle artifacts on the electroencephalogram (EEG) of hyperactive children referred for poor school performance, these irregular, arrhythmic muscle jerks of short duration were termed choreiform movements by Prechtl and Stemmer (1962). In a study of 50 children, age 9–12, with 90 percent exhibiting reading retardation, Prechtl and Stemmer (1962) reported a 100 percent incidence of choreiform movements of the tongue, face, neck, and trunk. Associated neurologic findings included hyperreflexia (88 percent) and abnormalities in muscle tone in a quarter of the children. These investigators thought the history of one or more prenatal or perinatal complications in 66 percent of the patients to have etiologic significance and raised the possibility of a causal relationship between the neurologic and the behavioral and learning phenomena. In a longitudinal study of infants born following complications of pregnancy or delivery, and reexamined at the ages of 2–4 years, 30 of 137 children were noted to demonstrate the choreiform syndrome (Prechtl and Dijkstra 1960). Of this group, 97 percent also had a positive history of cardiac or respiratory irregularities in the perinatal period or associated with severe pertussis. The perinatal events were hypothesized to be causative factors and the choreiform syndrome the outward manifestation of minimal brain damage. In an attempt to replicate this work, Rutter, Graham, and Birch (1966) were not able to determine a relationship between the choreiform syndrome and other minor neurologic abnormalities, reading problems, teacher ratings, or pregnancy complications. While the movements were found to be a reliable sign, there was great variability with no abrupt cutoff from the normal. This finding tended to occur more often in low IQ children (not significantly), boys, and younger children, but the clinical significance remained in doubt. Rutter, Graham, and Birch (1966) suggest that the failure of Prechtl and Dijkstra (1960) to consider IQ may have resulted in their having evaluated a mildly retarded rather than simply a learning disabled group. In another large-scale study, Wolfe and Hurwitz (1966), using choreiform movements as indicators of CNS dysfunction, noted that 17 percent of elementary school boys demonstrated such movements in contrast to 38 percent of juvenile delinquents and 28 percent of learning-disabled children. However, these investigators took note of jerky movements of the fingers, arms, and shoulder girdle in contrast to Prechtl and Stemmer (1962), who included movements of the tongue, eyes, head, and trunk as well as the upper limbs.

The discrepancies noted among the foregoing studies purportedly investigating the same phenomenon typify the state of attempts to relate minor neurologic abnormalities to behavioral and learning attributes. Even when the same neurologic finding is assessed across studies, the lack of precision and consistency in selection of control and target populations on the one hand, and the failure to measure the neurologic signs in a standardized manner on the other make comparisons between different investigations tenuous.

Most commonly employed measures of neuromaturational irregularity (soft signs) stem from attempts to capture "signs," no matter how subtle, of brain damage and thus reflect findings initially observed in a brain-injured population. In an example of this circular reasoning, Lord (1937) described perceptual, academic, and behavioral problems in children with cerebral palsy—difficulties that were assumed to be the result of the same cerebral insult that produced the motor handicap. These behavioral and educational deficits were then equated with brain damage and became indirect evidence for such CNS injury. Carried to its extreme, this reasoning led to the generalization that all patients demonstrating similar problems, even if they showed no abnormalities in the traditional neurologic examination, were to be considered as brain damaged. At present, the literature is inconclusive as to the significance of the presence of these minor abnormalities. This area has been comprehensively reviewed by Rutter (1977), who points out that brain damage is associated with increased risks of psychiatric disorder but not necessarily any specific or stereotyped behavioral syndrome. He also emphasizes the difficulties in validating brain damage. Instances of known CNS insult, as exemplified by encephalitis or trauma, remain rare events in the general population; other attempts to correlate historical occurrences and psychological or EEG test results with behavioral or cognitive functioning demonstrate inconsistent relationships leading to the conclusion that the current state of knowledge is yet insufficient to relate behavior and minor neurological function reliably to one another or to the structural properties and processes of the brain.

Current Status of the Yale Neuromaturational Examination (appendix 4). We have deliberatedly assumed the role of devil's advocate in emphasizing the caveats that clinicians and investigators should be aware of in order to provide a more accurate frame of reference with which to assess the significance of the presence of minor neurologic abnormalities in their own patients and in the literature. While the interpretation of many of the reports describing soft signs remains controversial, studies such as those of Peters, Romine, and Dykman (1975) suggest that there is merit to inclusion of the neuromaturational examination in children with behavioral and learning problems.

What are the requirements of such an examination? First and foremost, it must be a *developmental* neuromaturational examination for, after all, the disorders of behavior and learning under consideration occur in the developing nervous system. In contrast to the mature nervous system, the child's nervous system is dynamic, constantly in a state of flux in which many phenomena change with time. For example, synkinetic (associated) movements are normal in the young child but would be considered to be a minor neurologic abnormality in the adolescent. Yet, established age norms for the spectrum of developmental neurologic functions are either lacking or vary from one study to another. Not only is the brain a complex organ, but we are interested in tapping a broad representation of the more highly integrated of these functions, usually precluding our reliance upon the direct assessment of brain functions offered by the traditional neurologic examination. Instead, the examination for minor neurologic abnormalities attempts to assess higher cognitive processes in which responses are mediated by other integrative functions and subject to influences by an array of determinants such as attention, motivation, and impulsivity as well as environmental factors. The important influence of multiple determinants for each response underscores the necessity for maximization of variable control and standardization of environmental conditions. It dictates that rather than make inferences, reports of the findings of the neuromaturational examination clearly indicate the condition and the response, and also the child's behavioral state (attention, cooperation) during the examination.

We have attempted to develop an instrument, in the form of a standardized, developmentally sensitive procedure, for the detection and detailing of neuromaturational deviation among groups of children. To this end, we surveyed relevant psychiatric, neurodevelopmental, and psychological literature for potential items. Competing dictums of practicality in terms of efficiency of administration and comprehensiveness were considered and often arbitrary decisions made. To maximize reliability, criteria for selection of an individual item centered on ease of administration and scoring so that items producing a quantifiable response that could be assessed by objective criteria were given emphasis. Any function that could be quantified (measured in time or quantity) was preferred over those in which only subjective criteria could be used. Where such objective measurement was not possible, instead of dichotomous (normal-abnormal) appraisal of function, a series of precise descriptors was included to assess the varying functions tapped by a single item such as rhythm, habituation, and presence of associated movements. Preference was given to items that tended to recur in the literature and offered potential to discriminate clearly between children with behavioral and those with learning disorders. An attempt was made to tap a wide variety of neurological functions, including simple and complex gross and fine motor skills, laterality concepts, visual-motor proficiency, visual memory, choreiform movements, finger agnosia, diadochokinesis, and extinction, as well as to offer the examiner an opportunity to observe the child over a span of time performing basic, academically relevant graphomotor tasks. Items were selected that would further refine developmental appraisal of nervous system functioning so that a baseline level might be established as an index of current neuromaturational status and could also be used for serial evaluations so that changes, reflecting possible therapeutic intervention, might be measured.

Although concepts of brain-behavior relationships continue to evolve, the notion that, in children with disorders of behavior or cognition, the examination for minor neurologic abnormalities offers a window on CNS functioning continues to intrigue investigators. Thus, the last 40 years have witnessed a seemingly unending series of attempts to delineate minor abnormalities of the neurological examination in children; it was hoped these abnormalities might have heuristic value in furthering the understanding of behavior and learning difficulties, although just what these findings of irregularities on neuromaturational examination indicate has often been unclear. For the most part, these investigations have been flawed by poor methodology, including a lack of uniformity in describing abnormalities or determining their presence or absence, inadequate control groups, and failure to consider the effects of intelligence, social class, and other environmental factors. More importantly, there has existed a vagueness in interpreting the significance of the findings reported. Thus, from time to time, the findings of minor neurologic abnormalities have been used to indicate pathogenesis—some clinicians equating these findings with the diagnosis of brain *damage* or organicity, and others interpreting these signs as merely suggesting brain *dysfunction*. However, both the theoretical and practical limitations of such an approach are well recognized (*vide supra*). In our view, we would be reluctant to imbue the neuromaturational examination with any value in indicating the genesis of a particular symptom. Rather, we have developed a comprehensive neuromaturational examination with potential to use the presence of these abnormalities (1) to characterize and discriminate groups of children with assorted behavioral and learning difficulties, (2) as signals or predictors of a variety of neuropsychiatric disorders, and (3) to obtain an overview or profile of both optimal and suboptimal areas of CNS function.

Behavioral Process

Complementary to the Yale Neuromaturational Examination, the Yale Behavior Rating Scale (YBRS; see appendix 5) was developed in an attempt to capture some of those qualities of process and behavioral organization that may be the final determinants of a child's success or failure in the performance of any one particular task. The transactional model of behavioral-environmental relationships (Sameroff and Chandler 1975) suggests a central role for these operational styles in determining the product of the neurobehavioral dyad at any one time. Thus, a profile of factors of attention, adaptability, concentration, impulsivity, reflectivity, activity, and social awareness may be more insightful and relevant to understanding a child's functioning than a quantitative score on a specific test item. Thus, in the highly complex functions that psychological, neuromaturational, and academic tests tap, the output or resultant response (score) may be more a reflection of that child's unique style of operation than of the quality that task is alleged to measure. For example, particularly in children with attention deficit disorder, poor performance on the Arithmetic subtest of the Wechsler Intelligence Scale for Children (WISC–R) may be more reflective of attentional difficulties (Stevens et al. 1967) than of a lack of mathematical aptitude. Similarly, failure to stand on one foot for the suggested time interval is often noted in impulsive children who have no difficulties with spontaneous coordinated gross motor movements. The YBRS consists of 26 items that tap components of impulsivity, activity, relatedness, receptive and expressive language, attention, and consistency of performance.

In addition to its usage in conjunction with the Yale Neuromaturational Examination, the YBRS offers professionals in many fields (medicine, psychology, education) who interact with children with subtle neuropsychiatric disturbances a vehicle that serves to convey their observations in a precise, systematic, and uniform manner. Such behavioral profiles not only will have value in facilitating the interpretation of the child's performance on the neuromaturational examination but will add still another dimension in providing a multifactorial basis for the possible determination of homogeneous subgroupings among the heterogeneous population of children with less severe disorders of behavior and learning.

Developed with special sensitivity toward difficulties of children with attention deficit disorder, the YBRS may prove especially useful in psychopharmacologic studies to identify possible subgroups of children who may be candidates for drug therapy and then to monitor their response in a consistent manner.

Not infrequently, children who are doing poorly in their school work are referred for evaluation and found to show a discrepancy between quite good skills on the one hand and poor classroom performance on the other. In this situation, where the whole does not appear to represent the sum of its parts, it may be that the information provided by the YBRS on the child's processing capabilities will add balance to the equation. Thus, instead of a direct one-to-one correspondence between academic skills and school performance, it is the additional factor of how the child processes the material that becomes critical. These behavioral qualities, referred to as conceptual tempo by Becker (1976), were indeed found to have prognostic significance in determining academic achievement. Thus, in a cohort of kindergarten children, such behaviors as attention, effort, and self-confidence were determined to be related to later academic achievement in fifth grade. Becker reasons that while the specific skills required for success in the classroom vary from grade to grade, the behavioral competencies necessary for achievement are relatively stable over time. Similarly, predictive validity for a preschool assessment incorporating measures of both behavioral adaptation and neuromaturational status has been reported by Levine et al. (1980) for late kindergarten functioning.

The YBRS was designed in response to a need for a comprehensive, standarized instrument that might convey attributes of process that serve to characterize disabled children at school and during evaluation procedures. This 26-item behavioral questionnaire provides for four operationally defined levels of competence. The format uses items that are concise, yet, as often as possible, anchored by rich descriptors that seek to capture a specific quality relevant to the child's behavioral organization, particularly one that might be sensitive to change during drug intervention studies. To foster consistency and ultimately reliability, the scoring of each item is based on descriptive ratings that are objective rather than inferential in nature.

As with the neuromaturational examination, the YBRS offers potential utility in a variety of research strategies. In general, the YBRS will allow for the accumulation of data concerning behavioral correlates of success or failure on a particular task or test, or in overall classroom functioning. Such a profile could be useful in classifying groups of children, predicting school performance, and assessing change during psychopharmacologic studies. In our initial field trials, the YBRS has received acceptance from psychiatrists, neurologists, and pediatricians, as well as educators and psychologists.

Summary

Biologic research into neuropsychiatric disorders requires operationally defined, reliable, and valid diagnostic criteria. There is optimism that *DSM-III*, using a generally accepted nomenclature and specifying both inclusion and exclusion criteria, may provide the framework for such a consistent and reliable diagnostic schema. Yet remaining, however, is a mechanism for the orderly processing of the mass of clinical material into a format compatible with *DSM-III* constructs so that there is uniformity in determining whether criteria have or have not been met. In this communication, we have described a strategy to reconcile or bridge the large amount of clinical information from multiple dimensions, often subjective in nature, with the precise, dichotomous determinations (criteria have/have not been met) required by this diagnostic approach so that reliable and valid diagnosis will emerge from this process.

The YNPEAS provide a detailed plan for the systematic, focused, multidisciplinary investigation of neuropsychiatric disturbances in childhood. In each domain relevant to a child's functioning, historical and clinical findings are organized into operational statements that will ensure consistency across disciplines as well as across and within diagnostic groups. This information is coded for immediate entry into our computer system, further contributing an economy and orderliness to the research process. This approach, using structured, systematic methodology should result in the production of consistent, quantifiable data that will both lead to a rich picture of individual children and to a more integrated and comprehensive understanding of the basic principles underlying development and pathology.

We believe that the YNPEAS represents a significant step forward in the diagnostic process; for the first time to our knowledge, a diagnostic schema with operationally defined critiera has been linked to a tool for eliciting relevant information based on this schema. This represents but a first step toward the goal of reliable and valid diagnosis in neuropsychiatry and there is much to be done. The YNPEAS represents a first approximation and will no doubt be subject to modification. At this juncture we are completing a pilot study to determine the reliability and efficacy of this instrument. We have been gratified by its ease of administration and comprehensiveness. In these early trials we have found the YNPEAS to provide the uniformity and consistency sought, but also to allow for flexibility and to enhance rather than minimize clinical intuition.

Irrespective of the research strategy in clinical neuropsychiatry, there has been a need for a mechanism to gather information from multiple domains that could be efficiently translated into sets of relevant and consistent data, meaningful to investigators within and across specialities. The YNPEAS appears to fulfill this requirement; whether it will, indeed, contribute to a deeper understanding of these perplexing disorders awaits future investigations.

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Appendix 1. Yale Neuropsychoeducational Assessment Scales — Children's Personal Data Inventory

A. I.D.

Child's Personal Data Inventory:

— — — — 1-4
0 2 0 0 5-8
0 1 9-10

1. Date sent to informant .... __/__/__ mo. da. yr. 11-16

2. Child's birthdate .... __/__/__ mo. da. yr. 17-22

3. Child's sex ....

Male	1	
Female	2	23

4. Child's race ....

Caucasian	1	
Black	2	
Oriental	3	
Other	4	24

If other, specify ____________________

5. Child's siblings:
(Continue on back of page if necessary.)

Age In Years	Sex		Relation to this child			
	M	F	Full	Half	Step	
	1	2	1	2	3	25-26
	1	2	1	2	3	27-28
	1	2	1	2	3	29-30
	1	2	1	2	3	31-32
	1	2	1	2	3	33-34

6. This child lives:

With both parents	1	
With single parent	2	
With mother and stepfather	3	
With father and stepmother	4	
With relatives who are not parents	5	
With a foster family	6	
With adoptive parent(s)	7	
In a treatment facility	8	49

If treatment facility, specify type: ____________________

7. If the child was adopted, at what age: — — or — — —
yrs. mos. 50-52

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_ _ _ _ 0 2 0 0 0 2 1–10

B. General Medical History

1. Has this child ever had:

			If yes, at what age			
	No	Yes	0–2½ yrs.	2½–5 yrs.	6+ yrs.	
Encephalitis	1	2	2	2	2	11–14
Measles	1	2	2	2	2	15–18
Meningitis	1	2	2	2	2	19–22
Poisoning or overdose	1	2	2	2	2	23–26
Salmonella infection	1	2	2	2	2	27–30
Coma	1	2	2	2	2	31–34
Convulsions, seizures, epilepsy	1	2	2	2	2	35–38
Tremors	1	2	2	2	2	39–42
Head injuries	1	2	2	2	2	43–46
Migraine headaches	1	2	2	2	2	47–50
Anemia	1	2	2	2	2	51–54
Asthma	1	2	2	2	2	55–58
Eczema	1	2	2	2	2	59–62
Vision problems	1	2	2	2	2	63–66
Hearing problems	1	2	2	2	2	67–70

_ _ _ _ 0 2 0 0 0 3 1–10

Frequent ear infections	1	2	2	2	2	11–14
Psoriasis	1	2	2	2	2	15–18
Pneumonia	1	2	2	2	2	19–22
Hypothyroid	1	2	2	2	2	23–26
Hyperthyroid	1	2	2	2	2	27–30
Urinary problems	1	2	2	2	2	31–34
Other	1	2	2	2	2	35–38

If other, specify: ______________________________

	No	Yes	
2. Has this child been diagnosed as allergic to anything	1	2	39

If yes, allergic to:

	No	Yes	
Foods	1	2	40
Drugs	1	2	41
Dusts or pollens	1	2	42
Other	1	2	43

If other, specify: ______________________________

Treated by:

	No	Yes	
Diet	1	2	44
Antihistamines	1	2	45
Shots	1	2	46
Other	1	2	47

If other, specify: ______________________________

3. Has this child had an operation:

No	Yes	
1	2	48

If yes, describe the reason for each operation and give the age:

Reason:	Age in yrs. or mos.		
			49–51
			52–54
			55–57

4. Has this child ever been hospitalized for medical reasons other than for an operation:

No	Yes	
1	2	58

If yes, describe the reason for admission and give the age:

Reason:	Age in yrs. or mos.		
			59–61
			62–64
			65–67

_ _ _ _ 0 2 0 0 0 4 1–10

5. Has this child ever been to the emergency room or treated by a physician because of an accidental injury:

No	Yes	
1	2	11

If yes, describe each accident and give the age:

Accident:	Age in yrs. or mos.		
			12–14
			15–17
			18–20
			21–23
			24–26

6. Has this child ever been unconscious:

No	Yes	
1	2	27

If yes, describe the circumstances and give the age:

Circumstances:	Age in yrs. or mos.		
			49–51
			52–54
			55–57

7. *For females*: Has this girl begun to menstruate:

No	Yes	
1	2	37

If yes, at what age did she begin:

10 or younger	1	
11 through 15	2	
16 or older	1	38

8. *For males*: Has this boy reached puberty (growth of body hair, shaves, growth spurt):

No	Yes	
1	2	39

_ _ _ _ 0 2 0 0 0 5 1–10

C. Treatment History

1. What are the reasons for this child's current evaluation:

	No	Yes	
Physical problem	1	2	11
Speech problem	1	2	12
Hearing problem	1	2	13
Poor school work	1	2	14
Behavior problem at school	1	2	15
Behavior problem at home	1	2	16
immaturity	1	2	17
Emotional problem	1	2	18
Other	1	2	19

If other, specify: ____________________

2. How long have these problems been evident:

2 mos. or less	1	
3–6 mos.	2	
7–12 mos.	3	
More than 12 mos.	4	20

3. Do you feel that there was any particular disorder or problem that preceded the child's current problem and might have been associated with its onset:

No	Yes	21
1	2	22

If yes, describe: ____________________

4. Who felt that this child should be seen professionally at *this* time:

Pediatrician	01	
Family doctor	02	
Psychiatrist	03	
Neurologist	04	
Psychologist	05	
Education specialist outside of school	06	
Social worker	07	
School psychologist	08	
School social worker	09	
Teacher	10	
School nurse	11	
Pupil placement team (PPT)	12	
Family	13	
Other	14	23–24

If other, specify: ____________________

5. Has this child been evaluated previously for these or other related problems by any of the following? If yes, give age at the time of the evaluation, reason for the evaluation, diagnosis, and treatment.

By whom	Age in yrs.	Reason	Diagnosis	Treatment	
Pediatrician					25
Family doctor					26
Psychiatrist					27
Neurologist					28
Psychologist					29
Education specialist outside of school					30
Social worker					31
School psychologist					32
School social worker					33
Teacher					34
School nurse					35
Pupil placement team (PPT)					36
Other					37

If other, specify: ______________________________

6. Has this child received any of the following diagnoses:

	No	Yes	
Immature, maturation lag	1	2	38
Slow learner	1	2	39
Retarded	1	2	40
Autistic	1	2	41
Aphasic or language difficulty	1	2	42
Hyperkinetic, hyperactive	1	2	43
Minimal brain dysfunction (MBD)	1	2	44
Brain damaged	1	2	45
Learning disabled	1	2	46
Atypical	1	2	47
Depressed	1	2	48
Other	1	2	49

If other, specify: ____

7. Has this child received any of the following treatments for these problems:

	No	Yes	
Psychological therapy	1	2	50
Family counseling	1	2	51
Group therapy	1	2	52
After school tutoring	1	2	53
Special help in school	1	2	54
Special diet	1	2	55
Medication	1	2	56
Hospitalization	1	2	57
Other	1	2	58

If other, specify: ____

8. Has this child taken any of the following, and if so, at what ages:

	Age in Yrs	No	Yes	
Ritalin (methylphenidate)		1	2	59
Dexadrine		1	2	60
Phenobarbitol		1	2	61
Valium		1	2	62
Atarax		1	2	63
Antihistamine (to sedate or calm)		1	2	64
Dilatin		1	2	65
Tofranil (imipramine)		1	2	66
Haldol (halopridol)		1	2	67
Depekane (valproate)		1	2	68
Tegretol		1	2	69
Cylert (penoline)		1	2	70

D. Prenatal and Birth History

_ _ _ _ 0 2 0 0 0 6 1–10

Note: If this child is adopted, answer question 1 only and then skip to section E.
If the child is not adopted, then skip to question 2.

1. Were there any problems:

	No	Yes	Unknown	
During pregnancy	1	2	3	11
During delivery	1	2	3	12

At birth, how much did this child weigh: _ _/_ _ lbs. ozs. 13–16

Note: The following questions would best be answered by the natural mother of this child. If she is not available, the informant should answer those questions he/she can.

State why the natural mother is not available: ____________________

2. How old was the mother when this child was born: _ _ yrs. 17–18

3. How old was the father when this child was born: _ _ yrs. 19–20

4. How many pregnancies did you have *before* the pregnancy with this child (including unsuccessful pregnancies): 21–22

5. Did you have any miscarriages or stillbirths before the birth of this child:

No	1	
1	2	
2 or more	3	23

6. Were any of the pregnancies before this child delivered prematurely:

No	1	
1	2	
2 or more	3	24

7. Which one of the following birth control methods did you use just before your pregnancy with this child:

None	1	
Birth control pills (specify type and dose)	2	
Intrauterine device	3	
Diaphragm	4	
Male contraceptive	5	
Other (specify)	6	25

If pills or other, specify ____________________

8. When did you stop using the above contraceptive:

More than a year before conception	1	
3 months to a year before conception	2	
Never stopped or less than 3 months before conception	3	26

9. Did you take fertility drugs just before your pregnancy with this child:

No	Yes	
1	2	27

10. Did you have any of the following during your pregnancy with this child? If yes, state the *circumstances*, the specific *drugs* (if any) taken, and the *trimester* of pregnancy involved (1, 2, or 3).

	Circumstances	Name of Drug	Trimester	No	Yes	
Morning sickness				1	2	28
Bleeding from the vagina				1	2	29
Premature contractions				1	2	30
Swelling (edema) of face, hands, ankles				1	2	31
High blood pressure				1	2	32
Incompatible Rh factor				1	2	33
Toxemia				1	2	34
Rubella				1	2	35
Diabetes				1	2	36
Anemia				1	2	37
Serious injury				1	2	38
Emotional problems				1	2	39
Other illness				1	2	40
X-rays				1	2	41
Blood pressure pills				1	2	42
Tranquilizers or sedatives				1	2	43
Pills for nausea				1	2	44
Antibiotics				1	2	45
Water pills (diuretic)				1	2	46
Medication for pain				1	2	47
Medication to prevent miscarriage				1	2	48
Medication to prevent weight gain				1	2	49
More than 10 cigarettes per day				1	2	50
Two or more drinks per day (alcohol)				1	2	51
Three or more cups of coffee/tea per day				1	2	52
Valium				1	2	53
Prednisone				1	2	54
Amphetamine				1	2	55
Methadone				1	2	56
Marijuana				1	2	57
Thyroid medication				1	2	58
LSD				1	2	59
Cocaine				1	2	60
Heroin				1	2	61
Other drugs				1	2	62

Note: Did you give the specific information for any "yes" responses?

11. How much weight did you gain with this child:

Under 20 lbs.	1	
21–30 lbs.	2	
Over 30 lbs.	3	63

12. Did you have to stay in bed for more than 3 days during your pregnancy with this child:

No	Yes	
1	2	64

13. Was amniocentesis performed (a sample of fluid was taken from the womb):

No	Yes	
1	2	65

If yes, why: ______

14. Was this pregnancy unusual or abnormal in any way not already mentioned:

No	Yes	
1	2	66

If yes, in what way: ______

0 2 0 0 0 7 — — — — 1–10

15. Did any of the following things occur at or following the delivery of this child:

	No	Yes	
Premature delivery (more than 2 wks. early)	1	2	11
Late delivery (more than 2 wks. overdue)	1	2	12
Labor was induced by drugs	1	2	13
Cesarean section was performed before onset of labor	1	2	14
Cesarean section was performed after onset of labor	1	2	15
General anesthesia was used (mother was unconscious)	1	2	16
Local anesthesia was used (a spinal block)	1	2	17
The doctor said labor was prolonged	1	2	18
Breech delivery (buttocks first)	1	2	19
Use of forceps	1	2	20
Cord around neck	1	2	21
Blue at birth	1	2	22
Slow heartbeat	1	2	23
Didn't breath at first	1	2	24
Infant had seizure fits or convulsions	1	2	25
Infant had jaundice (yellow in color)	1	2	26
Infant jittery	1	2	27
Infant had unusual cry	1	2	28
Infant required oxygen	1	2	29
Infant required blood transfusion	1	2	30
Infant was placed in an incubator	1	2	31
Twin or multiple birth	1	2	32
Other problem	1	2	33

If other, specify: ______

16. How long was labor:

2 hrs or less	1	
3–12 hrs.	2	
12–24 hrs.	3	
More than 24 hrs.	4	34

17. At birth, how much did this child weigh: __ __ / __ __ lbs. ozs. 35–38

18. How soon after delivery did you get to hold, feed or play with this child in a usual way:

first day	1	
2–7 days	2	
8 or more days after birth	3	39

19. Did child stay in the hospital after you left:

No	Yes	
1	2	40

If yes, why: ________________________________

If yes, how old was he/she when allowed to go home:

Under 2 wks.	1	
2–4 wks.	2	
5–10 wks.	3	
Over 10 wks.	4	41

20. Were your first children breastfed? List all your children with this child first:

Child:	No	Yes			Why did you stop?	
		1–7 Days	2–6 Wks.	7+ Wks.		
This child	1	2	3	4		42
	1	2	3	4		43
	1	2	3	4		44
	1	2	3	4		45
	1	2	3	4		46
	1	2	3	4		47

(Continue on back if necessary.)

_ _ _ _ 0 2 0 0 0 8 1–10

E. First Months

Note: The following questions pertain to the first few months of life of this child's growth up to about six mos. old.

1. Did this child:

Want to be held a great deal of the time	1	
Want to be held sometimes and not at others	2	
Appear indifferent to being held	3	
Resist being held	4	11

2. How predictable were this child's sleeping habits:

Mostly predictable	1	
More predictable than unpredictable	2	
More unpredictable than predictable	3	
Mostly unpredictable	4	12

3. Did this child:

	No	Yes	
Have difficulty falling asleep	1	2	13
Have difficulty staying asleep	1	2	14
Awaken frequently	1	2	15
Have difficulty awakening	1	2	16

4. Did this child:

Sleep most of the time and need to be awakened for feedings	1	
Sleep mostly between feedings but awaken when hungry	2	
Sleep between some feedings but fairly long periods of wakefulness	3	
Sleep very little and seem comfortable	4	
Sleep little and seem comfortable most of the time	5	17

5. During the first months of life, how predictable were this child's eating habits:

Mostly predictable	1	
More predictable than unpredictable	2	
More unpredictable than predictable	3	
Mostly unpredictable	4	18

6. Did this child:

	No	Yes	
Have difficulty sucking	1	2	19
Have a poor appetite	1	2	20
Have difficulty swallowing	1	2	21
Spit up frequently	1	2	22
Appear to be insatiably hungry	1	2	23
Have other difficulty eating	1	2	24

If other, specify: ____________________

7. During the first months, how difficult did you find this child to care for:

Very difficult	1	
Difficult	2	
Somewhat difficult	3	
Not very difficult	4	25

8. Was this child:

Extremely active	1	
Normally active	2	
Inactive and quiet but alert	3	
Sluggish and nonresponsive	4	26

9. Was this child:

Easily upset by sights and sounds	1	
Highly attentive to sights and sounds	2	
Moderately attentive to sights and sounds	3	
Unresponsive to sights and sounds	4	27

10. Did this child fuss and cry:

Most of the time	1	
Often	2	
Occasionally	3	
Hardly ever	4	28

11. Was this child:

Very difficult to comfort	1	
Difficult to comfort	2	
Somewhat difficult to comfort	3	
Not very difficult to comfort	4	29

12. During the first months, did any of the following occur:

	No	Yes	
Child was diagnosed as having colic	1	2	30
Changed formulas frequently	1	2	31
Medication was prescribed to calm or soothe the baby	1	2	32

If yes, what medication:

F. 6 mos. to 2½ yrs.

Note: The following questions pertain to the time after the first months of life to age 2½.

	No	Yes	
1. During ages 6 mos. to 2½ yrs., did this child reach out and prepare to be picked up when approached by mother.	1	2	33

2. Was this child's behavior:

The same as other children	1	
Like older children	2	
Like younger children	3	
Different but not older or younger	4	34

3. Did this child:

Want to be held a great deal of the time	1	
Want to be held sometimes and not at others	2	
Appear indifferent to being held	3	
Resist being held	4	35

4. How predictable were this child's sleeping habits:

Mostly predictable	1	
More predictable than unpredictable	2	
More unpredictable than predictable	3	
Mostly unpredictable	4	36

5. How predictable were this child's eating habits:

Mostly predictable	1	
More predictable than unpredictable	2	
More unpredictable than predictable	3	
Mostly unpredictable	4	37

6. During ages 6 mos. to 2½ yrs., did this child:

Never attempt to communicate	1	
Rarely use either gestures or language to communicate	2	
Frequently use gestures but rarely use language to communicate	3	
Use language to communicate	4	38

7. During ages 6 mos. to 2½ yrs., how did this child react to light, sound, or smell:

Strong reaction	1	
Moderate reaction	2	
Appeared not to notice	3	39

If strong reaction, was the child:

Distressed	1	
Happy	2	40

8. How did this child react to pain or injury:

Strong reaction	1	
Moderate reaction	2	
Appeared not to notice	3	41

_ _ _ _ 0 2 0 0 0 9 1–10

G. Developmental Landmarks

Note: For each of the following events in this child's development, indicate the age at which it happened and whether you felt this was early, on time, or late for a child to be learning this skill. Check *Not Applicable* if the skill has not been learned yet.

1. When did this child:	Age in yrs. or mos.		Not appl.	Early	On time	Late	
Smile at parents			1	2	3	4	11–14
Sit alone			1	2	3	4	15–18
Walk with assistance			1	2	3	4	19–22
Walk without assistance			1	2	3	4	23–26
Speak first words			1	2	3	4	27–30
Speak 2- to 3-word phrases or sentences			1	2	3	4	31–34
Speak such that most people understand			1	2	3	4	35–38
Eat with utensils			1	2	3	4	39–42
Respond to his/her name			1	2	3	4	43–46
Understand names of objects			1	2	3	4	47–50
Obey verbal commands			1	2	3	4	51–54
Show ability to be sent on an errand or with a message			1	2	3	4	55–58
Go downstairs			1	2	3	4	59–62
Get dressed by him/herself			1	2	3	4	63–66
Tie shoelaces			1	2	3	4	67–70

_ _ _ _ 0 2 0 0 1 0 1–10

Ride a 2-wheeled bike without training wheels			1	2	3	4	11–14
Complete daytime urinary training			1	2	3	4	15–18
Complete nighttime urinary training			1	2	3	4	19–22
Complete daytime bowel training			1	2	3	4	23–26
Complete nighttime bowel training			1	2	3	4	27–30

	No	Yes	
2. Did this child begin to speak and then stop talking altogether:	1	2	31

If yes, at what age did this child stop: yrs. or mos. 32–34

	No	Yes	
Has speech begun again:	1	2	35

If yes, at what age did this child begin again: yrs. or mos. 36–38

	No	Yes	
3. Did this child begin bed/pants wetting a yr. or more after urinary training was complete:	1	2	39

If yes, at what age did the wetting begin: yrs. or mos. 40–42

Has wetting stopped:

No, still occurs at least once a mo.	1
Yes, by 5 yrs. old	2
Yes, by 6–9 yrs. old	3
Yes, by 10 or older	4

43

4. Did this child begin bed/pants soiling a year or more after bowel training:

No	Yes
1	2

44

If yes, at what age did the soiling begin:

_____ yrs. or _____ mos. 45–47

Has soiling stopped:

No, still occurs at least once a month	1
Yes, by 5 yrs. old	2
Yes, by 6–9 yrs. old	3
Yes, by 10 or older	4

48

5. Is this child:

Right handed	1
Left handed	2
Uses either hand	3

49

6. In general, during early childhood (2½–5 yrs. old), was this child:

Well coordinated	1
Somewhat coordinated	2
Somewhat clumsy	3
Very clumsy	4

50

_ _ _ _ 0 2 0 0 1 1 1–10

Note: Indicate how difficult or easy the following activities were for this child to learn and how well he/she performs them now. If the skill was never attempted for whatever reason (handicap, child is too young), check *Not applicable*.

7. Activity:

	Learning				Performing					
	Easy	Not too difficult	Somewhat difficult	Very difficult	Very well	Fairly well	Not too well	Poor to unable	Not appl.	
Eat with utensils	1	2	3	4	1	2	3	4	99	11–12
Get dressed by himself	1	2	3	4	1	2	3	4	99	13–14
Do buttons and zippers	1	2	3	4	1	2	3	4	99	15–16
Tie shoes	1	2	3	4	1	2	3	4	99	17–18
Print letters	1	2	3	4	1	2	3	4	99	19–20
Draw	1	2	3	4	1	2	3	4	99	21–22
Play with Legos	1	2	3	4	1	2	3	4	99	23–24
Fine hand work in general such as puzzles, models	1	2	3	4	1	2	3	4	99	25–26
Swim	1	2	3	4	1	2	3	4	99	27–28
Skateboard	1	2	3	4	1	2	3	4	99	29–30
Play baseball and/or football	1	2	3	4	1	2	3	4	99	31–32
Play soccer	1	2	3	4	1	2	3	4	99	33–34
Tell time	1	2	3	4	1	2	3	4	99	35–36
Count money	1	2	3	4	1	2	3	4	99	37–38
Recognize numbers	1	2	3	4	1	2	3	4	99	39–40
Recognize letters	1	2	3	4	1	2	3	4	99	41–42

	No	Yes	
8. Does this child ride a two-wheel bike without training wheels:	1	2	43

If no, is it because this child:

	No	Yes	
Isn't ready yet — too young	1	2	44
Just couldn't learn	1	2	45
Falls off	1	2	46
Is afraid of heights	1	2	47
Other	1	2	48

	No	Yes	
9. Does this child play well in group games:	1	2	49

If no, is it because this child:

	No	Yes	
Lacks coordination	1	2	50
Can't take turns	1	2	51
Gets confused by the rules	1	2	52
Gets overstimulated and uncontrolled	1	2	53
Doesn't pay attention–daydreams	1	2	54
Other	1	2	55

If other, specify: ____________________

____

_ _ _ _ 0 2 0 0 1 2 1–10

H. Communication

Note: The following are lists of characteristics of speech. For the 2 age groups, indicate whether the characteristic is never true or sometimes, often, or almost always true.

	No	Yes
Has this child begun to speak (if no, skip to section I):	1	2

1. During ages 2½–5, did this child:	Never	Some-times	Often	Almost always	
Speak very little; communicate his/her needs only	1	2	3	4	11
Stutter or stammer	1	2	3	4	12
Hesitate or stop midsentence	1	2	3	4	13
Seem to understand but have trouble getting the words out	1	2	3	4	14
Have difficulty finding the right word	1	2	3	4	15
Confuse the order of words, such as "Ball, I hit"	1	2	3	4	16
Confuse words of opposite meaning, such as yesterday/tomorrow	1	2	3	4	17
Confuse words that sound alike, such as hem/hen	1	2	3	4	18
Refer to himself by name, such as "Joe go to store"	1	2	3	4	19
Speak in his/her own private language	1	2	3	4	20
Show an inability to tell about what happened to him, such as about his day	1	2	3	4	21

2. During ages 6 and over, did this child (if child is not yet 6, skip to section I):	Never	Some-times	Often	Almost Always	
Speak very little; communicate his/her needs only	1	2	3	4	22
Stutter or stammer	1	2	3	4	23
Hesitate or stop midsentence	1	2	3	4	24
Have difficulty finding the right word	1	2	3	4	25
Confuse the order of words, such as "Ball, I hit"	1	2	3	4	26
Confuse words of opposite meaning, such as yesterday/tomorrow	1	2	3	4	27
Confuse words that sound alike such as hem/hen	1	2	3	4	28
Speak as if under great pressure; words come out explosively	1	2	3	4	29
Have trouble pronouncing words	1	2	3	4	30

_ _ _ _ 0 2 0 0 1 3   1–10

I. Habits

Note: The following is a list of characteristics concerning sleeping and eating habits and organizational ability. Indicate if the characteristic was never true of this child or if it was true during ages 2½–5, 6–9, or 10 yrs. and older. Ignore ages that are not appropriate to this child.

1. Does this child:

	No	Yes	If yes			
			2½–5 Yrs.	6–9 Yrs.	10+ Yrs.	
Have difficulty falling asleep	1	2	2	2	2	11–14
Have difficulty getting up and going in morning	1	2	2	2	2	15–18
Need a lot of sleep	1	2	2	2	2	19–22
Need very little sleep	1	2	2	2	2	23–26
Frequently awaken during the night	1	2	2	2	2	27–30
Show signs of physical activity while asleep	1	2	2	2	2	31–34
Rise and wander during the night	1	2	2	2	2	35–38
Go on rampages at night, emptying drawers, icebox	1	2	2	2	2	39–42
Have frequent nightmares	1	2	2	2	2	43–46
Need mother's presence to fall asleep	1	2	2	2	2	47–50
Frequently sleep in parents' bed	1	2	2	2	2	51–54
Have poor appetite	1	2	2	2	2	55–58
Have difficulty swallowing	1	2	2	2	2	59–62
Choke on food	1	2	2	2	2	63–66
Vomit after eating	1	2	2	2	2	67–70

_ _ _ _ 0 2 0 0 1 4   1–10

Show insatiable hunger; hungry in less than ½ hr. after eating	1	2	2	2	2	11–14
Crave sweets, other particular foods	1	2	2	2	2	15–18
Refuse most foods	1	2	2	2	2	19–22
Wolf food quickly	1	2	2	2	2	23–26
Wander from table between mouthfuls	1	2	2	2	2	27–30
Have bedroom and toys totally disorganized; inability to order things	1	2	2	2	2	31–34
Insist that bedroom and toys must be precisely ordered	1	2	2	2	2	35–38
Have inability to keep to a schedule	1	2	2	2	2	39–42
Always dress in a disorderly fashion, with shoes or buttons undone	1	2	2	2	2	43–46
Approach projects illogically; do things the hard way	1	2	2	2	2	47–50

2. This child is:

Highly organized	1	
Moderately organized	2	
Somewhat disorganized	3	
Very disorganized	4	51

_ _ _ _ 0 2 0 0 1 5   1–10

J. Behavioral Characteristics

Note: For each of the following behaviors, indicate if it was characteristic of this child at no time or during age 0–2½, 2½–5, or 6 and older. Ignore age groups that are not applicable to this child and those ages that have been shaded out.

1. Did or does this child:	No	Yes	If yes			
			0–2½ yrs.	2½–5 yrs.	6+ yrs.	
Have parrotlike quality to speech; repeat statements mechanically	1	2	2	2	2	11–14
Have singsong quality to speech	1	2	2	2	2	15–18
Speak in a whisper	1	2	2	2	2	19–22
Laugh or giggle for no apparent reason	1	2	2	2	2	23–26
Cover ears at many sounds	1	2	2	2	2	27–30
Show signs of being deaf	1	2	2	2	2	31–34
Have temper tantrums	1	2	2	2	2	35–38
Have breath holding	1	2	2	2	2	39–42
Have frequent or prolonged crying	1	2	2	2	2	43–46
Rock in crib or bed	1	2	2	2	2	47–50
Bang head	1	2	2	2	2	51–54
Smear stools	1	2	2	2	2	55–58
Pick skin; pull hair, pluck eyebrows or lashes	1	2	2	2	2	59–62
Hit or bite self	1	2	2	2	2	63–66
Bite nails	1	2	2	2	2	67–70

_ _ _ _ 0 2 0 0 1 6   1–10

Grind teeth	1	2	2	2	2	11–14
Seem not to be able to learn from experience, even if hurt	1	2	2	2	2	15–18
Chew or bite objects; eat strange substances, such as plaster or garbage	1	2	2	2	2	19–22
Cling excessively to mother	1	2	2	2	2	23–26
Prefer to be alone; show lack of interest in people; withdraw	1	2	2	2	2	27–30
Show no attachment to parents	1	2	2	2	2	31–34
Show indifference to affection	1	2	2	2	2	35–38
Dislike being held or touched	1	2	2	2	2	39–42
Avoid eye contact	1	2	2	2	2	43–46
Behave as if other person not there	1	2	2	2	2	47–50
Have unusual ability such as repeating jingles, recalling dates, doing puzzles, perfect pitch	1	2	2	2	2	51–54
Show attachment to odd objects	1	2	2	2	2	55–58
Engage in rituals	1	2	2	2	2	59–62
Hold odd beliefs not based on reality	1	2	2	2	2	63–66
Have special fears he/she avoids such as heights, dogs, undressing	1	2	2	2	2	67–70

_ _ _ _ 0 2 0 0 1 7   1–10

See visions or hear voices not seen or heard by others	1	2	2	2	2	11–14
Stare at lights, water, or shiny objects as if entranced	1	2	2	2	2	15–18
Show excessive fear or anxieties	1	2	2	2	2	19–22
Have strong aversion to being wet or dirty	1	2	2	2	2	23–26

Repeat words, phrases, or actions over and over as if driven	1	2	2	2	2	27–30
Have an unusual odor	1	2	2	2	2	31–34
Whirl in circles	1	2	2	2	2	35–38
Walk on toes	1	2	2	2	2	39–42
Drool	1	2	2	2	2	43–46
Assume the role of a clown	1	2	2	2	2	47–50
React violently to minor changes in environment or routine	1	2	2	2	2	51–54
Respond in bizarre ways to normal events	1	2	2	2	2	55–58
Have a blank expression; stare for long periods	1	2	2	2	2	59–62
Show lack of awareness of where he/she is; or the time of day	1	2	2	2	2	63–66
Fail to appreciate danger; show tendency to be fearless, even reckless	1	2	2	2	2	67–70

_ _ _ _ 0 2 0 0 1 8 1–10

2. Do you have to dress this child exceptionally well to make him/her appear more socially acceptable:

No	Yes	
1	2	11

3. Has this child ever had vocal or physical tics such as:

	No	Yes	
Clearing throat, grunting, barking, yelping, snorting	1	2	12
Uttering words, phrases, or curses involuntarily	1	2	13
Twitches, jerks, or tics	1	2	14

If yes, could this child suppress the tics:

No	Yes	
1	2	15

Did the intensity or frequency of the tics vary over the weeks:

No	Yes	
1	2	16

How long did the tics last:

Less than 1 mo.	1	
1 mo. to 1 yr.	2	
More than 1 yr.	3	17

4. Has this child ever had frequent headaches, stomachaches, nausea, or dizziness with no apparent medical basis:

No	Yes	
1	2	18

If yes, which: ______________________________

Did they seem to occur:

Mostly in the morning	1	
Mostly in the afternoon	2	
Mostly in the evening	3	
Mostly at night	4	
At varied times	5	19

Did they occur only or mostly on schooldays:

No	Yes	
1	2	20

5. Has this child been depressed, sad, down in the dumps:

Never	1	
Rarely	2	
Sometimes	3	
Often	4	21

If sometimes, or often, is it:

Mostly in the morning	1	
Mostly in the afternoon	2	
Mostly in the evening	3	
Mostly at night	4	
At varied times	5	22

Did the depression or sadness begin shortly after the death of someone close or a pet:

No	Yes	
1	2	23

Does the depression or sadness go away when a parent is with this child:

No	Yes	
1	2	24

Note: The following are lists of characteristic behaviors. Indicate which are never true of this child or rarely, sometimes, or often true.

6. For ages from birth up to 6 yrs. old:	Never	Rarely	Sometimes	Often	
Climbed onto cabinets and furniture	1	2	3	4	25
Was always on the go; would run rather than walk	1	2	3	4	26
Broke toys and other things; was destructive	1	2	3	4	27
Couldn't keep hands to self	1	2	3	4	28
Demanded adult company	1	2	3	4	29
Required unusual confinement (harness, gates)	1	2	3	4	30
Couldn't tolerate a noisy, busy place; would go wild in a crowd	1	2	3	4	31
Was very difficult to take for a visit to friends	1	2	3	4	32
Was very difficult to leave with a babysitter	1	2	3	4	33
Was very difficult to take shopping	1	2	3	4	34
Needed constant supervision	1	2	3	4	35

7. For ages 6 or older, this child (if this child is not yet 6, skip to question 8):	Never	Rarely	Sometimes	Often	
Hums or taps his/her fingers	1	2	3	4	36
Takes a long time to settle down in a new place or activity	1	2	3	4	37
Does things without thinking; is impulsive	1	2	3	4	38
Talks too much	1	2	3	4	39
Fidgets or squirms	1	2	3	4	40
Bumps into things; gets into accidents	1	2	3	4	41
Demands adult company	1	2	3	4	42
Is never satisfied; constantly wants things	1	2	3	4	43
Does things in a loud and noisy way	1	2	3	4	44
Must always be doing something or becomes fidgety	1	2	3	4	45
Can play quietly for 20 minutes or more	1	2	3	4	46
Dawdles	1	2	3	4	47
Does things in a painfully slow way	1	2	3	4	48
Daydreams	1	2	3	4	49
Is hyperactive	1	2	3	4	50
Is hypoactive, yawns frequently; has little energy; is placid	1	2	3	4	51
Resists change in the routine; must know the day's schedule in advance	1	2	3	4	52
Is overly cautious	1	2	3	4	53
Cries for slightest reason	1	2	3	4	54
Is not aware of social rules of modesty (boy has fly open; girl has dress up)	1	2	3	4	55

_ _ _ _ 0 2 0 0 1 9 1–10

8. In general, at any age how characteristic of this child were these behaviors:	Never	Rarely	Sometimes	Often	
Is forgetful	1	2	3	4	11
Confuses the details	1	2	3	4	12
Forgets or loses his belongings (mittens, lunchbox)	1	2	3	4	13
Needs a calm, quiet atmosphere in order to work or concentrate	1	2	3	4	14
Does sloppy work even though he/she tries hard	1	2	3	4	15
Changes activities frequently; flits	1	2	3	4	16
Is indecisive; changes mind over and over again	1	2	3	4	17
Is impatient, can't wait in line; has to have what he/she wants now	1	2	3	4	18
Doesn't finish what he/she starts (a book, puzzle)	1	2	3	4	19
Given a choice, he/she picks the first	1	2	3	4	20
Can't sit through a board game; wants to change games	1	2	3	4	21
Can't tolerate frustration	1	2	3	4	22
Hears but doesn't seem to listen	1	2	3	4	23
Has no guilt for doing wrong or hurting others	1	2	3	4	24
Has excessive guilt or feels guilty at inappropriate times	1	2	3	4	25
Rules don't get through to him/her	1	2	3	4	26
Doesn't respond to reasonable persuasion	1	2	3	4	27
Can't seem to learn from experience	1	2	3	4	28
Can't tell right from wrong	1	2	3	4	29
Must be in control of the situation	1	2	3	4	30
Must do things "my way"; can't be taught how to do things	1	2	3	4	31
Cheats; has to be the winner	1	2	3	4	32

Blames others for errors; always has an excuse	1	2	3	4	33
Complains of unfair treatment; everyone is against him/her	1	2	3	4	34
Worries	1	2	3	4	35
Is pessimistic; always thinks things will go badly	1	2	3	4	36
Has a poor self-image; feels worthless	1	2	3	4	37
Attempts or talks of harming self	1	2	3	4	38
Is bored	1	2	3	4	39
Overly concerned about how well he/she is doing in school, sports	1	2	3	4	40
Has rapid unexpected mood changes	1	2	3	4	41
Is irritable	1	2	3	4	42
Has a short fuse; explodes at any little thing	1	2	3	4	43
Has hurt someone so that he/she required medical attention	1	2	3	4	44
Is insensitive to the feelings of others	1	2	3	4	45
Gets into arguments	1	2	3	4	46
Provokes adults	1	2	3	4	47
Is defiant; is belligerant when corrected or disciplined; resists authority	1	2	3	4	48
Is stubborn	1	2	3	4	49
Doesn't argue but doesn't do what he/she is told	1	2	3	4	50
Purposely does opposite of what he/she is told	1	2	3	4	51
Makes up stories	1	2	3	4	52
Can't be trusted on his/her own	1	2	3	4	53
Is aggressive but only if person is younger or weaker	1	2	3	4	54
Hangs around with a bad crowd	1	2	3	4	55
Extends him/herself only if it is an advantage to him/herself	1	2	3	4	56
Extends him/herself even where there is no advantage to him/herself	1	2	3	4	57
Is a "sponger" (takes favors with no effort to return them)	1	2	3	4	58

9. How was this child with unfamiliar adults:

Not at all friendly	1	
Somewhat friendly	2	
Friendly	3	
Excessively friendly	4	59

_ _ _ _ 0 2 0 0 2 0   1–10

10. For the following, indicate how many times this has occurred. This child:	0	1	2	3+	
Ran away from home overnight	1	2	3	4	11
Killed or tortured animals	1	2	3	4	12
Set a fire	1	2	3	4	13
Stole things other than from family members	1	2	3	4	14
Was arrested, in court or in jail	1	2	3	4	15
Was sent from home because of behavior problems	1	2	3	4	16
Was the cause of complaints from the neighbors about behavior	1	2	3	4	17
Was the cause of complaints from the school about behavior	1	2	3	4	18
Stayed out past curfew	1	2	3	4	19
Smoked tobacco	1	2	3	4	20
Got drunk or stoned	1	2	3	4	21
Used pot, heroin, or other drugs; sniffed glue	1	2	3	4	22

11. Did any of the following occur over an *extended period of time* (6 mos. or more):

	No	Yes	
Swearing, use of vulgar language	1	2	23
Lying to other than family members	1	2	24
Cruelty to younger children not limited to siblings: bullying	1	2	25
Stealing of things other than from family members	1	2	26
Vandalism	1	2	27
Violence and aggression, assaults on others, fighting	1	2	28
Moving traffic violations, such as speeding, reckless driving	1	2	29
Extortion, forcing someone under threat of harm	1	2	30
Breaking and entering	1	2	31

12. In order to do chores and obey parental rules, would you describe this child as:

Needing no supervision	1	
Needing an occasional reminder	2	
Needing frequent reminders	3	
Needing constant supervision	4	32

13. This child:

Never steals or breaks rules	1	
Will only steal or break rules if he/she thinks no one is around	2	
May even steal or break rules when he/she is supervised	3	
Even steals or breaks rules while he/she is closely supervised	4	33

	No	Yes	
14. Does this child have any hobbies	1	2	34

If yes, specify: ______________________________

	No	Yes	
15. Does this child belong to any clubs or groups (scouts, teams, band):	1	2	35
If yes, are the groups for special children:	1	2	36

What is this child's favorite activity: ______________________________

What is this child's least liked activity: ______________________________

_ _ _ _ 0 2 0 0 2 1 1-10

K. Peer Interactions

Note: During ages 2½ through 5, how did this child interact with other children? Indicate on the following list if the characteristic is true of this child never, rarely, sometimes, or often.

1. This child:	Never	Rarely	Sometimes	Often	
Wants friends but provokes them to anger	1	2	3	4	11
Wants friends but is rejected or avoided by other children	1	2	3	4	12
Hurts children by being rough or physical	1	2	3	4	13
Is bossy with other children	1	2	3	4	14
Takes children's toys or food	1	2	3	4	15
Gets feelings hurt easily by children	1	2	3	4	16
Gets physically hurt by children	1	2	3	4	17
Enjoys being with other children	1	2	3	4	18
Chooses to play with children of the opposite sex	1	2	3	4	19
Chooses activities associated with the opposite sex	1	2	3	4	20

Note: During ages 6 and older, how did the child interact with other children? Indicate on the following list if the statement is or is not characteristic of this child. If this child is not yet 6 years old, skip to question 3.

2. This child:	No	Yes	
Wants friends but is rejected or avoided by children	1	2	21
Chooses to play with children of the opposite sex	1	2	22
Tends to associate with children with "problems"	1	2	23
Has had a "close" friend	1	2	24
Has no close friends but plays well in a group	1	2	25
Has had friendships that lasted more than 6 mos.	1	2	26
Can't keep up with children his own age	1	2	27
Wants friends, but provokes them to anger	1	2	28
Wants friends, but leads them into trouble	1	2	29
Is loyal to his friends; will not inform on his friends	1	2	30
Informs on his friends easily	1	2	31
Is cold and untrusting of other children	1	2	32
Gets into fights with other children because he/she is easily frustrated	1	2	33
Is overly submissive; is easily led by others	1	2	34
Has to be the leader in games	1	2	35
Disrupts other children's games or activities	1	2	36

3. Generally, does this child choose to play with:

Children about the same age	1	
Much younger children	2	
Much older children	3	
Adults	4	37

4. At any age, would you say this child:

	No	Yes	
Has many friends and is well liked	1	2	38
Does not seem to care if he/she has friends	1	2	39
Has very few or no friends	1	2	40

Appendix 2. Yale Neuropsychoeducational Assessment Scales—School and Family Information Form

_ _ _ _ 0 2 5 0 0 1 1–10
Date: _ _ _ _ _ _ 11–16
DOB: _ _ _ _ _ _ 17–22

L. School

Note: If this child has not gone to school yet, skip to section M.

1. At what age did this child start nursery school or daycare: __ or ___ ___ yrs. mos. 23–25

2. At what age did this child start kindergarten: __ or ___ ___ yrs. mos. 26–28

3. What grade is this child in now: ___ ___ 29–30

4. When this child started school, did you expect any problems:

	No	Yes	
	1	2	31

If yes, what problems and why: ________________________________

____

5. Once this child had been attending school regularly did he/she:

	Never	Rarely	Sometimes	Often	
Cry about going	1	2	3	4	32
Refuse to go	1	2	3	4	33
Complain of being ill in order not to go	1	2	3	4	34
Appear frightened or anxious about going	1	2	3	4	35
Arrive at school late	1	2	3	4	36
Stay home from school	1	2	3	4	37

6. Has this child ever:

	No	Yes	
Skipped a grade	1	2	38
Been held back a grade	1	2	39
Attended a special residential school	1	2	40
Attended a special day school	1	2	41
Attended special education classes	1	2	42
Attended a resource room	1	2	43
Received tutoring in school	1	2	44
Received tutoring after school	1	2	45
Received remedial reading	1	2	46
Received speech or language therapy	1	2	47
Attended special gym	1	2	48
Received perceptual training	1	2	49
Attended a program for the gifted	1	2	50

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If attended a special school, was it for:

	No	Yes	
Behavioral or emotional problems	1	2	51
Learning disability	1	2	52
Language disability	1	2	53
Physical disability	2	2	54

	No	Yes	
7. Has the school ever requested help in managing this child:	1	2	55

8. This child has problems with:

	No	Yes	
Reading	1	2	56
Spelling	1	2	57
Handwriting	1	2	58
Composition	1	2	59
Math	1	2	60
Science	1	2	61
Social Studies	1	2	62
Speech	1	2	63
Other	1	2	64

If other, specify: ______________________________

____

_ _ _ _ 0 2 5 0 0 2 1–10

9. Below is a list of characteristics pertaining to school and school work. From your experience working with this child on school work or from information obtained in report cards or in conferences, indicate whether the characteristic is true never, rarely, sometimes or often. Though some of the characteristics are the same as those listed earlier these should be limited to behavior related to school. If you don't know about a particular item check *Never; Don't Know*.

	Never; Don't Know	Rarely	Sometimes	Often	
Is slow to complete school work	1	2	3	4	11
Is slow to complete projects he chooses himself such as art or shop	1	2	3	4	12
Homework seems to go on all night	1	2	3	4	13
Quality of work varies from day to day	1	2	3	4	14
Fails to turn in homework	1	2	3	4	15
Avoided doing homework	1	2	3	4	16
Avoided written work	1	2	3	4	17
Failed to check over his work	1	2	3	4	18
Avoided participation in class	1	2	3	4	19
Seemed to lack interest in school; seemed to lack motivation	1	2	3	4	20
Had difficulty concentrating or paying attention unless in 1:1 structured situation	1	2	3	4	21
Seemed to work better in the morning	1	2	3	4	22
Seemed to work better in the afternoon	1	2	3	4	23

Been unable to pace work on long assignments	1	2	3	4	24
Needed supervision or failed to complete assignments	1	2	3	4	25
Been unable to adjust to other children	1	2	3	4	26
Disrupted other children	1	2	3	4	27
Been unable to adjust to new situations	1	2	3	4	28
Been unable to adapt to changes in routine	1	2	3	4	29
Had mood fluctuations usually unrelated to situation	1	2	3	4	30
Had trouble waiting his turn	1	2	3	4	31
Been very active in class	1	2	3	4	32
Failed to listen in class	1	2	3	4	33
Talked excessively	1	2	3	4	34
Called out in class; made noises in class	1	2	3	4	35
Been extremely excitable	1	2	3	4	36
Been slow to respond	1	2	3	4	37
Gotten lost within the school building	1	2	3	4	38
Asked to have things repeated	1	2	3	4	39
Been easily distracted	1	2	3	4	40
Been easily frustrated	1	2	3	4	41
Been unruly and argumentative	1	2	3	4	42
Lost control on the playground, or the bus, or in the lunchroom	1	2	3	4	43
Gotten into fights	1	2	3	4	44
Had trouble with sequences such as the alphabet or numbers	1	2	3	4	45
Used incomplete sentences or made grammatical errors	1	2	3	4	46
Had difficulty copying from a book	1	2	3	4	47
Had difficulty lining up math problems	1	2	3	4	48
Confused the order of numbers	1	2	3	4	49
Jumbled or reversed letters or syllables in a word, words in a sentence	1	2	3	4	50
Gotten mixed up, lost his place when reading	1	2	3	4	51
Pronounced words incorrectly	1	2	3	4	52
Been unable to tell a comprehensible story	1	2	3	4	53

10. This child approaches his school work:

In a well-organized manner	1	
Usually in an organized manner	2	
Usually in a disorganized manner	3	
In a totally disorganized manner	4	54

	0	1	2	3+	
11. How many times has this child been suspended or expelled:	1	2	3	4	55
12. How many times has this child played hooky (been truant):	1	2	3	4	56

_ _ _ _ 0 2 5 0 0 3 1–10

M. Family Information

1. Who is the principal wage earner in the household:

Father	1	
Mother	2	
Other or not applicable	3	

For whom do the parents work and in what capacity:

Father ____

Mother ____ 11–12

How far did the father go in school ____________________________ 13–14

How far did the mother go in school ____________________________ 15–16

Marital status of the parents:

Single	1	
Married	2	
Separated	3	
Divorced	4	
Widowed	5	17

If informant is not this child's natural parent, what is the relationship:

Grandparent	1	
Aunt or uncle	2	
Sibling	3	
Foster parent	4	
Adoptive parent	5	
Stepparent	6	
Other	7	18

The following questions should be answered about this child's natural family. If the informant is not familiar with the natural parents, grandparents, and siblings, then the questions should be answered with respect to the child's current family. Answers should be confined to one set of relatives only.

The following information concerns the:

Natural family	1	
An adoptive or foster family	2	
No information; the child does not live with a family	3	19

The next 9 pages present a grid like the example given below for each of the following groups of persons: this child's brothers and sisters; this child's father and his family; and this child's mother and her family. For each group write in the names of the family members across the top as shown for Aunt Mary and Uncle Bill below. Then for each of the persons put a check in the box below his/her name that corresponds to each condition the person has (as, for example, Aunt Mary has asthma). Leave boxes blank for conditions that person does not have (as, for example, Aunt Mary does not have diabetes), and for inappropriate questions (as, for example, school questions for a preschool age child).

Medical:

			Uncles							Aunts					
Mother's Family	Mother	Grandfather	Bill						Grandmother	Mary					
Left handed or used both hands	√	√								√					
Had high blood pressure			√						√						
Had asthma										√					
Had migraine			√												
Had thyroid problems	√									√					
Had diabetes									√						
Had seizures or epilepsy		√													
Was mentally retarded															

Note: Mother refers to this child's mother. Grandfather here refers to this child's mother's father and grandmother refers to this child's mother's mother. Uncles and aunts refer here to this child's mother's brothers and sisters.

I. **Brothers and Sisters of Child**

Write in the names and check the appropriate boxes.

		Brothers						Sisters						
														20–21
Medical:	Left handed or used both hands													22–23
	Had high blood pressure													24–25
	Had asthma													26–27
	Had migraine													28–29
	Had thyroid problems													30–31
	Had diabetes													32–33
	Had seizures or epilepsy													34–35
	Was mentally retarded													36–37
In school:	Had trouble reading													38–39
	Had trouble with math													40–41
	Had trouble speaking (stuttering, poor articulation)													42–43
	Had trouble spelling													44–45
	Had trouble with foreign languages													46–47
	Had trouble learning — a slow learner													48–49
	Had very poor handwriting													50–51
	Had trouble completing school work													52–53
	Had problems listening or hearing													54–56

Had problems understanding and remembering directions, phone nos.												
Confused right and left												
Attended special classes or schools												
Stayed back a year in school or failed more than 1 course												
Skipped a grade in school												

__ __ 56–57

__ __ 58–59

__ __ 60–61

__ __ 62–63

__ __ 64–65

_ _ _ _ 0 2 5 0 0 4 1–10

As children:

Were hyperactive												
Were clumsy or awkward												
Were poor athletes												
Were overactive or restless												
Had behavior problems — hard to control												
Were in trouble with the authorities — expelled from school												
Were arrested, taken before a judge, in jail												
Were immature acting — crybabies, excessively shy												
Were still wetting the bed after 5 yrs. old												

__ __ 11–12

__ __ 13–14

__ __ 15–16

__ __ 17–18

__ __ 19–20

__ __ 21–22

__ __ 23–24

__ __ 25–26

__ __ 27–28

As adults:

Had employment problems — changed jobs frequently													____ 29–30
Had drinking problems													____ 31–32
Had drug problems													____ 33–34
Were arrested, taken before a judge, in jail													____ 35–36
Became depressed, suicidal													____ 37–38
Had a nervous breakdown													____ 39–40
Sought professional help for an emotional problem													____ 41–42
Enjoyed drinking nightly													____ 43–44

N. Father's Family

Write in the names and check the appropriate boxes.

				Uncles							Aunts						
		Father	Grand-father							Grand-mother							
Medical:	Left handed or used both hands																— — — 45–46
	Had high blood pressure																— — — 47–49
	Had asthma																— — — 50–52
	Had migraine																— — — 53–55
	Had thyroid problems																— — — 56–58
	Had diabetes																— — — 59–61
	Had seizures or epilepsy																— — — 62–64
	Was mentally retarded																— — — 65–67
																	— — — 68–70

In school:	Had trouble reading																— — — — 0 2 5 0 0 5 1–10
	Had trouble with math																— — — 11–13
	Had trouble speaking (stuttering, poor articulation)																— — — 14–16
	Had trouble spelling																— — — 17–19
	Had trouble with foreign languages																— — — 20–22
	Had trouble learning — a slow learner																— — — 23–25
	Had very poor handwriting																— — — 26–28
	Had trouble completing school work																— — — 29–31
	Had problems listening or hearing																— — — 32–34
																	— — — 35–37

Had problems understanding and remembering directions, phone nos.																	38–40
Confused right and left																	41–43
Attended special classes or schools																	44–46
Stayed back a grade or failed more than 1 course																	47–49
Skipped a grade in school																	50–52

_ _ _ _ 0 2 5 0 0 6 1–10

As children:

Were hyperactive																	11–13
Were clumsy or awkward																	14–16
Were poor athletes																	17–19
Were overactive or restless																	20–22
Had behavior problems — hard to control																	23–25
Were in trouble with the authorities — expelled from school																	26–28
Were arrested, taken before a judge, in jail																	29–31
Were immature acting — crybabies, excessively shy																	32–34
Were still wetting the bed after 5 yrs. old																	35–37

As adults:

Had employment problems — changed jobs frequently																38–40
Had drinking problems																41–43
Had drug problems																44–46
Were arrested, taken before a judge, in jail																47–49
Became depressed, suicidal																50–52
Had a nervous breakdown																53–55
Sought professional help for an emotional problem																56–58
Enjoyed drinking nightly																59–61

_ _ _ _ 0 2 5 0 0 7 1-10

III. Mother's Family

Write in the names and check the appropriate boxes.

				Uncles							Aunts						
		Mother	Grand-father							Grand-mother							11–12
Medical:	Left handed or used both hands																13–15
	Had high blood pressure																16–18
	Had asthma																19–21
	Had migraine																22–24
	Had thyroid problems																25–27
	Had diabetes																28–30
	Had seizures or epilepsy																31–33
	Was mentally retarded																34–36
In school:	Had trouble reading																37–39
	Had trouble with math																40–42
	Had trouble speaking (stuttering, poor articulation)																43–45
	Had trouble spelling																46–48
	Had troubles with foreign languages																49–51
	Had trouble learning — a slow learner																52–54
	Had very poor handwriting																55–57
	Had trouble completing school work																58–60
	Had problems listening or hearing																61–63

Had problems understanding and remembering directions, phone nos.																64-66
Confused right and left																67-69

— — — — 0 2 5 0 0 8 1-10

As children:

Attended special classes or schools																11-13
Stayed back a grade or failed more than 1 course																14-16
Skipped a grade in school																17-19
Were hyperactive																20-22
Were clumsy or awkward																23-25
Were poor athletes																26-28
Were overactive or restless																29-31
Had behavior problems — hard to control																32-34
Were in trouble with the authorities — expelled from school																35-37
Were arrested, taken before a judge, in jail																38-40
Were immature acting — crybabies, excessively shy																41-43
Were still wetting the bed after 5 yrs. old																44-46

As adults:

Had employment problems — changed jobs frequently																47–49
Had drinking problems																50–52
Had drug problems																53–55
Were arrested, taken before a judge, in jail																56–58
Became depressed, suicidal																59–61
Had a nervous breakdown																62–64
Sought professional help for an emotional problem																65–67
Enjoyed drinking nightly																68–70

Appendix 3. Yale Neuropsychoeducational Assessment Scales—Stigmata Schedule

Anomaly Scoring:

I.D. __ __ __ __ 1–4
0 5 0 0 5–8
0 1 9–10

1. Today's date: ___/___/___ 11–16
mo. da. yr.

2. Child's birthdate: ___/___/___ 17–22
mo. da. yr.

3. Examining physician: ______________ ___ 23

4. Height: mms ___ ___ ___ 24–27

Code: (H≤1.0 SD) (1.0 SD<H≤1.5 SD) (1.5 SD<H)

1	2	3	28

5. Weight: kg ___ ___ 29–32

Code: (W≤1.0 SD) (1.0 SD<W≤1.5 SD) (1.5 SD<W)

1	2	3	33

6. Head circumference: mms ___ 34–36

Code: (C≤1.0 SD) (1.0 SD<C≤1.5 SD) (1.5 SD<C)

1	2	3	37

7. ICC distance: mms ___ 38–39

Code: (see chart in protocol)

1	2	3	40

8. Palpebral fissures: mms ___ 41–42

9. Naso-vermillion border distance: mms ___ 43–44

10. Eye color: 45

Blue	1
Brown	2
Gray/green	3
Other	4

11. Hair color: 46

Brunette, dark brown	1
Ash blond, light brown	2
Red	3
Platinum, very pale blond, white	4

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Anomaly grading scale: Leave blank spaces for anomalies not actually checked.

		Normal or absent	Equivocal	Abnormal or present	
12. Hair	Frontal bossing:	1	2	3	47
	Whorls: (1) (<1 or a line ≥1" long)	1	2	3	48
	Electric hair: (Normal) (Fine; soon awry) (Very fine; will not comb)	1	2	3	49
	Coarse, brittle:	1	2	3	50
13. Eyes:	Strabismus:	1	2	3	51
	Ptosis:	1	2	3	52
	Crusting of lid:	1	2	3	53
	Epicanthus: (absent) (partial) (deep)	1	2	3	54
14. Ears:	Malformed	1	2	3	55
	Asymmetric:	1	2	3	56
	Pits or tags:	1	2	3	57
	Soft and pliable:	1	2	3	58
	Low set (above) (≤.5 cm below) (>.5 cm below) line thru nosebridge and eye	1	2	3	59
	Lobe extension: (below attachment) (straight back) (toward crown)	1	2	3	60

_ _ _ _ 0 5 0 0 0 2 1–10

15. Nose:	Antiverted nostrils:	1	2	3	11
	Hypoplastic tip:	1	2	3	12
	Hypoplastic philtrum:	1	2	3	13
16. Mouth:	Palate: (normal arch) (flat steeple ⌒) (high steeple ∩)	1	2	3	14
	Cleft palate — soft or hard:	1	2	3	15
	Tongue furrowed:	1	2	3	16
	Tongue with smooth-rough spots:	1	2	3	17
	Teeth — enamel hypoplasia; carious:	1	2	3	18
	Teeth small:	1	2	3	19
	Upper vermillion thin:	1	2	3	21
17. Jaw:	Prominent maxilla:	1	2	3	22
	Micrognathia:	1	2	3	23
	Prognathia:	1	2	3	24
	Midfacial hypoplasia:	1	2	3	25
18. Torso:	Webbed neck:	1	2	3	26
	Pectus excavatum:	1	2	3	27
	Pectus carinatum:	1	2	3	28
	Nipples widely spaced:	1	2	3	29
	Heart murmur:	1	2	3	30
	Vertebral defects:	1	2	3	31
	Hernia — umbilical, diaphragm, groin: diastasis recti	1	2	3	32
	Hypospadias:	1	2	3	33
19. Skin	Thin skin — visible vascular pattern:	1	2	3	34
	Dry, coarse, rough:	1	2	3	35
	Cafe-au-lait:	1	2	3	36
	Hemangiomata:	1	2	3	37
	Nails — hypoplastic or dysplastic:	1	2	3	38

20. Hands:	Palm — coarse skin:	1	2	3	39
	Palm — single transverse crease:	1	2	3	40
	Small, broad hands:	1	2	3	41
	Thin, tapering hands:	1	2	3	42
	Joint limitation:	1	2	3	43
	Clinodactyly:	1	2	3	44
	Broad first toe or thumb:	1	2	3	45
21. Feet:	Gap between first and second toes:	1	2	3	46
	Partial syndactylia of 2nd and 3rd toes:	1	2	3	47
	Length of 2nd and third toes: (2nd > 3rd) (2nd = 3rd) (2nd < 3rd)	1	2	3	48
22. Other:	Other anomaly:	1	2	3	49

If other, specify: ______________________________

____

Appendix 4. Yale Neuropsychoeducational Assessment Scales — Neuromaturational Examination

I.D. _ _ _ _ 1–4

0 4 0 0 5–8

0 1 9–10

A. Neuromaturational Examination:

1. Today's date: mo. da. yr. 11–16
2. Child's birthdate: mo. da. yr. 17–22
3. Examining physician: 23
4. Significant motor handicap or posturing:

No	1	24
Yes	2	

If yes, does it involve:	No	Right	Left	Both	
.... upper extremities	1	2	3	4	25
.... lower extremities	1	2	3	4	26
.... other	1	2	3	4	27

B. Balance

1. Passive motor stance — arms extended in front, on toes, 30′

Number of twitches of arms, fingers, hands, face, or eyes:

0,1	1	28
2–5	2	
6–10	3	
>10	4	
NA	5	

Deviations:

None	1	29
Slight	2	
Some; maintains stance with difficulty	3	
Marked; spooning; loss of stance	4	
NA	5	

General Scoring of Performance

1 = Correct: immediate correct response; smoothly performed.
2 = Hesitant: mild hesitation or impulsive but then correct; *at most* 1 false start.
3 = Poor: needs repeated instruction or changes response more than once.
4 = Unable: unable to perform; incorrect even after repeated instruction.
5 = NA: not assessed for whatever reason.

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2. Walk on heels — arms at side, 10 steps

Performance:

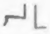
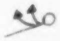
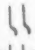
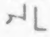
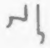
Correctly performed	1	30
Elbow flexion; wrist hyperextension	2	
Toes barely off floor; flailing	3	
< 4 steps	4	
NA	5	

3. Walk on toes — arms at side, knees straight, 10 steps

Performance:

Correctly performed	1	31
Elbow extension; wrist flexion	2	
Marked knee flexion and posturing	3	
< 4 steps	4	
NA	5	

	Correct	Hesitant	Poor	Unable	NA	
	Performance					
4. Tandem walk, forward:	1	2	3	4	5	32
Tandem walk, backward:	1	2	3	4	5	33

5. Age:	Eyes:	Arms:	Legs:	Time:		Correct	Hesitant	Poor	Unable	NA	
						Performance					
5+	0	↓↓		10'		1	2	3	4	5	34
6+	0	↓↓		10'	R	1	2	3	4	5	35
					L	1	2	3	4	5	36
7+	0			10'		1	2	3	4	5	37
8+	●	←→		10'		1	2	3	4	5	38
9+	●	↓↓		15'	R	1	2	3	4	5	39
					L	1	2	3	4	5	40
10+	●	↓↓		15'		1	2	3	4	5	41
11+	●	↓↓		10'	R	1	2	3	4	5	42
					L	1	2	3	4	5	43
11+	●	↓↓		10'	R	1	2	3	4	5	44
					L	1	2	3	4	5	45

C. **Finger Agnosia:** Practice 1 & 3

						4	3	2	1–0	NA	
						Number correct					
1. Pattern	2&4	3&5	2&5	2&3	R	1	2	3	4	5	46
Fingers in between	1	1	2	0	L	1	2	3	4	5	47
2. Pattern	4	2&3	4&5	3	R	1	2	3	4	5	48
Fingers touched	1	2	2	1	L	1	2	3	4	5	49

D. **Laterality:** 4 years

1. Hand: "Show me how you":

Brush your teeth
Throw a ball
Cut with scissors
Print
Eat with a spoon

All R	1	50
4,3R/1,2L	2	
2,1R/3,4L	3	
All L	4	
NA	5	

2. Eye: "Show me how you would look through a telescope".

3. Foot: "Show me how you kick a ball":

R	L	NA	
1	2	3	51
1	2	3	52

4. "Show me your": .... number correct

L hand
R eye
L ear
R hand

4	1	53
3	2	
2	3	
1–0	4	
NA	5	

"Show me your ________ with your ________": .... number correct

L ear/L hand
R eye/L hand
R knee/R hand
L eye/L hand
R ear/L hand
L knee/R hand
R ear/R hand
L eye/R hand

8	1	54
7–6	2	
5–4	3	
< 4	4	
NA	5	

"Show me my": .... number correct

R eye
L leg
L ear
R hand

"Show me my ________ with your ________":

L ear/R hand
R knee/L hand
L arm/L hand
L knee/R hand

8	1	55
7–6	2	
5–4	3	
< 4	4	
NA	5	

5. Performance of laterality:

Correct	1	56
Hesitant	2	
Poor	3	
Unable	4	
NA	5	

E. **Fine Motor**

1. Nose touch — "Touch your fingertip to the tip of your nose with your ________ hand."

	Correct	Hesitant	Poor	Unable	NA	
R	1	2	3	4	5	57
L	1	2	3	4	5	58

_ _ _ _ 0 4 0 0 0 2

2. Fingertap — "Can you tap your finger like this? When I say go, tap as fast as you can with your ____ hand." Time 20 taps

Seconds

R ___ . ___ 11–15

Average right ______ R ___ . ___ 16–20

L ___ . ___ 21–25

Average left ______ L ___ . ___ 26–30

Overflow:

	R	L	
None	1	1	31,32
Mild (flicker)	2	2	
Moderate (marked contralateral)	3	3	
Marked body involvement	4	4	
NA	5	5	

3. Successive finger tap — "Can you tap your fingers like this? When I say go, tap as fast as you can with your ____ hand." Time 5 rounds (Index to 5th finger)

Seconds

R ___ . ___ 33–37

Average right ______ R ___ . ___ 38–42

L ___ . ___ 43–47

Average left ______ L ___ . ___ 48–52

Overflow:

	R	L	
None	1	1	53,54
Mild	2	2	
Moderate (marked contralateral)	3	3	
Marked body involvement	4	4	
NA	5	5	

Rhythm:

Smooth	1	1	55,56
Stickiness; curling	2	2	
Frequent misses; disorganization	3	3	
Inability to perform	4	4	
NA	5	5	

4. Diodochokinesis

"Can you turn your hand back and forth like this, trying to move your wrist only?"

Overflow:

	R	L	
None	1	1	57,58
Mild	2	2	
Moderate (marked contralateral)	3	3	
Marked body involvement	4	4	
NA	5	5	

Discreteness:

Elbow moves <5 cm	1	1	59,60
Elbow moves 5-15 cm	2	2	
Shoulder and elbow move	3	3	
Marked generalized movement	4	4	
NA	5	5	

Rhythm:

Correct; smooth	1	1	61,62
Hesitant, lapses	2	2	
Rigid, awkward	3	3	
No resemblance to task	4	4	
NA	5	5	

5. Mouth and tongue involvement in the fine motor tasks:

None	1	63
Mild	2	
Moderate	3	
Marked	4	
NA	5	

6. Foot tap

"Can you tap your hands and feet like this?" 15'

	Correct	Hesitant	Poor	Unable	NA	
Coordinated tap - R hand & R foot; L hand & L foot (6+ years):	1	2	3	4	5	64
Complex tap - Hands & R foot; L foot (9+ years):	1	2	3	4	5	65

Habituation:

Begins smoothly; ends smoothly	1	66
Begins smoothly; rhythm, rate deteriorates	2	
Begins poorly; improves	3	
Never correct	4	
NA	5	

F. Sensation

"Close your eyes and tell me where I'm touching you."

L cheek/R hand
R cheek/L hand
L cheek/L hand
R cheek/R hand
cheek/cheek

hand/hand
L cheek/R hand
R cheek/L hand
L cheek/L hand
R cheek/R hand

number wrong

0	1	67
1–2	2	
3–4	3	
5+	4	
NA	5	

G. Object Span

_ _ _ _ 0 4 0 0 0 3

Age Set up	Pattern	Correct					
		Immediate	Hesitant	Partially	Incorrect	NA	
1. 5+; pen, coin, key	312	1	2	3	4	5	11
	213	1	2	3	4	5	12
2. 6+; pen, clip, key, coin	4132	1	2	3	4	5	13
	2431	1	2	3	4	5	14
3. 7+; pin, pen, clip, key, coin	51342	1	2	3	4	5	15
	42351	1	2	3	4	5	16
4. 9+; pin, pen, clip, key, coin, block	134625	1	2	3	4	5	17
	423561	1	2	3	4	5	18
5. 5+; three blocks	312	1	2	3	4	5	19
	213	1	2	3	4	5	20
6. 6+; four blocks	4132	1	2	3	4	5	21
	2431	1	2	3	4	5	22
7. 7+; five blocks	51342	1	2	3	4	5	23
	42351	1	2	3	4	5	24
8. 9+; six blocks	134625	1	2	3	4	5	25
	423561	1	2	3	4	5	26

H. Figure Drawing

1. "I'm going to ask you to copy two sets of pictures for me. I want you to copy them as well as you can. I will be timing you."

Representation:

Perfect at age level	1	27
Minor errors; spatial representation intact	2	
Poor at age level but good at year below	3	
Very poor at year below	4	
NA	5	

Time to complete picture at age level: _ _ _ . _ sec. 28–32

2. "Now draw a clock face for me with all the numbers, and show 3:30. Again, do as well as you can. I will be timing you." (7+)

Clock face:

Correct sequence and space	1	33
Correct sequence; poor spacing; digit reversal	2	
Correct sequence but continues on; all pushed to one side	3	
Incorrect sequencing; unrecognizable numbers	4	
NA	5	

3:30:

Correct	1	34
Hands reversed	2	
One hand wrong	3	
Both hands wrong	4	
NA	5	

Time to complete picture: . secs. 35–39

I. Writing

1. "Now I want you to write a row of numbers for me."

3 5 6 7 9

Good numbers and spacing	1	40
Good numbers: poor spacing	2	
Reversals; directionality confusion	3	
Unrecognizable	4	
NA	5	

2. "Now write a row of lower case [little] letters for me."

b d p q w z m n

Good letters and spacing	1	41
Good letters; poor spacing	2	
Reversals; directionality confusion	3	
Unrecognizable	4	
NA	5	

3. "Now I'm going to ask you to print a few sentences for me. Do as well as you can, but write quickly because I will be timing you."

6+ A boy had a dog.
6+ A dog saw a bird.
9+ My name is ____________.
9+ Please come quickly.
12+ The question is about the Constitution.

Time to complete sentences at age 6+: . secs. 42–46

Reversals or directional confusion:

No	1	47
Yes	2	
NA	3	

Spelling at age level:

No errors	1	48
Reversed sequence of letters	2	
Phonetically correct only	3	
Unrecognizable	4	
NA	5	

Dysgraphia:

Age-appropriate handwriting	1	49
Some uncertainty; confused letter attack	2	
Inconsistent size, shape, pressure	3	
Illegible, rushed, or painfully slow	4	
NA	5	

Peculiar approach to handwriting:

No	1	50
Yes	2	
NA	3	

J. Recognition

1. "Point to your ________":
2. "Tell me what I'm pointing to":

	Number wrong					
	0	1	2	3+	NA	
1.	1	2	3	4	5	51
2.	1	2	3	4	5	52

hair
hands
feet
ear
nose
knee
heel
forehead
cheek
chin
thumb
nails
shoulder
eyelashes
elbow
wrist
eyebrow
nostril
ankle
sole

Performance:

Correct	1	53
Hesitant	2	
Poor	3	
Unable	4	
NA	5	

K. Orientation

"Can you tell me . . .":

	Rapid recall	Hesitant recall	Recognition only	Neither	NA	
Your name:	1	2	3	4	5	54
Your address:	1	2	3	4	5	55
Town:	1	2	3	4	5	56
State:	1	2	3	4	5	57
Your telephone number:	1	2	3	4	5	58
Where you are today:	1	2	3	4	5	59
Day of the week:	1	2	3	4	5	60
Month of the year:	1	2	3	4	5	61
Year:	1	2	3	4	5	62
What is this (show the tape measure):	1	2	3	4	5	63

Appendix 5. Yale Neuropsychoeducational Assessment Scales: Behavior Rating Scale

I.D. _ _ _ _ 1–4
0 8 0 1 5–8
0 1 9–10
Today's date: __/__/__ mo. da. yr. 11–16
Child's birthdate: __/__/__ mo. da. yr. 17–22
Examiner: ______ 23

Characteristics	1	2	3	4	Fill in the #	
Impulsivity; acts or speaks without first thinking	Rare 1	Occasional 2	Often 3	Constant, unremittent 4		24
Fidgeting	Rare 1	Taps fingers or foot; hums 2	Squirms in seat 3	Out of the chair 4		25
Motor inhibitions; touches people or objects within reach	Keeps hands to self 1	Occasionally touches people and objects 2	Frequently touches people and objects 3	Must touch anything in sight 4		26
Motor activity; restlessness	Rarely restless 1	Occasionally seems restless 2	Often moves about 3	Driven; doesn't stop 4		27
Fatiguability	Alert 1	Occasionally appears tired 2	Tries to rest on self or props; some yawning 3	Expresses fatigue; slumps over; frequent yawning 4		28
Slow performance	Not at all slow 1	Occasionally slow 2	Markedly slow on some tasks 3	Markedly slow irrespective of task 4		29
Pressured or rushed performance	Not at all 1	Occasionally rushes through work 2	Often rushes 3	Always pressured; races on 4		30
Social awareness	Appropriate to age 1	Occasionally immature; giggly 2	Frequently inappropriate 3	Bizarre; unaware 4		31
Cooperation	Cooperative 1	Occasionally negative or reluctant to perform 2	Inconsistently negative; needs much urging 3	Oppositional; refuses completely 4		32
Reaction to or tolerance for frustration	Reacts appropriately 1	Slight anger or tearfulness 2	Moderate anger or tearfulness 3	Very angry or cries; marked lability 4		33
Ability to work independently	Able 1	Needs occasional reminder 2	Needs frequent prodding or encouragement to work 3	Work markedly impaired even with frequent prodding 4		34
Follows verbal directions	Appropriately 1	Needs occasional repetition 2	Requires demonstration 3	Unable to follow gestures or verbal commands 4		35
Knowledge and application of rules in academic work	Knows and applies rules 1	Minor inconsistency in knowing or applying rules 2	Seems to know rules but confuses application 3	Doesn't know or apply rules 4		36

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					Fill in the #	
Ability to listen	Listens intently 1	Needs occasional reminder to listen 2	Intermittent; misses parts 3	Doesn't listen 4		37
Monitoring, checks over work	Almost always 1	Often will self-correct 2	Rarely checks answers or work 3	Never monitors or checks work 4		38
Ability to "get started"	Starts work immediately 1	Slight hesitation before starting 2	Noticeable hesitation in specific areas 3	Always hesitates first before starting 4		39
Performance during any 1 assignment	Consistent; steady 1	Improves with time 2	Irregular; inconsistent 3	Deteriorates with time 4		40
Adaptive learning; ability to "catch on"	Quick; learns readily 1	Usually "gets it," occasional reexplanation required 2	Marked difficulties but may get it 3	Limited ability to learn new task 4		41
Persistence in approach to a difficult task	Persistent, keeps trying 1	Several attempts, then gives up 2	Few attempts, then quits 3	Gives up immediately 4		42
Distractibility	Ignores all irrelevant stimuli 1	Aware of irrelevant stimuli but continues to work 2	Frequently interrupts work due to irrelevant stimuli 3	Hypervigilant; distracted by slightest stimulus 4		43
Ability to focus in	Pays attention immediately 1	Occasional effort to get attention 2	Constant effort to get attention 3	Cannot get attention 4		44
Lapses in performance	None; smooth performance 1	Rare break or lapse in performance 2	Occasional break or lapse in performance 3	Frequently fades out; erratic 4		45
Expressive language ability	Fluent 1	Rare hesitation or pause 2	Circumlocution; long latencies; misspoken words 3	Marked retrieval difficulties; gropes for the right word 4		46
Ability to relate to adults	Warm 1	Occasional awkwardness 2	Atypical awkwardness 3	Bizarre; nonrelated 4		47
Ability to relate to other children	Warm 1	Occasional awkwardness 2	Atypical awkwardness 3	Bizarre; nonrelated 4		48

Family Factors in Schizophrenic Relapse: A Replication

by Christine E. Vaughn, Karen S. Snyder, William Freeman, Simon Jones, Ian R.H. Falloon, and Robert Paul Liberman

At Issue

Abstract

Family factors have been reported to influence the course of schizophrenia. In a replication of British studies, schizophrenic patients from the Los Angeles area were evaluated for symptomatic relapse 9 months after hospital discharge as a function of the level of "expressed emotion" in their relatives. In striking confirmation of the British findings, patients who came from families that were excessively critical, emotionally overinvolved, or both were much more likely to relapse than their counterparts who came from more tolerant and accepting families.

Although medication has been effective in reducing the duration of inpatient treatment for schizophrenia, serial admissions and relapse continue to dominate the lives of schizophrenic patients. Thus, interest has burgeoned concerning the influence of social and family factors and their association with symptomatic relapse and hospital readmission.

British studies on the influence of social and family factors on the course of schizophrenia have shown that symptomatic relapse is most likely if a patient lives with relatives who are characterized as being high on "expressed emotion" (EE). High EE reflects critical, hostile, and/or overprotective attitudes toward the patient. High EE is coded from in-depth, reliably rated interviews of family members at the time of a patient's hospitalization and, hence, serves as a predictor of risk for relapse. Patients whose relatives were high on EE were four times more likely to relapse during the 9 months following hospital discharge than patients whose relatives were rated as more accepting and less intertwined (Brown, Birley, and Wing 1972; Vaughn and Leff 1976).

At the Camarillo/UCLA Mental Health Clinical Research Center for the Study of Schizophrenia, a replication of the British work on EE was carried out with a sample of "Anglo" patients and families from the Los Angeles area. Like the British work, patients were diagnosed as schizophrenic on the basis of the Present State Examination and CATEGO criteria. Then, based on a standardized interview, the scales of EE—criticism, hostility, and overinvolvement—were rated for relatives of 54 recently hospitalized schizophrenics. Patients were closely followed for 9 months after discharge and rated monthly for relapse or exacerbation of symptoms.

Results of the study have confirmed the British findings of a significant association of patients living in high EE families and symptomatic relapse; in fact, the similarity of the data between England and California is striking (see table 1). Fifty-six percent of patients with a high EE relative suffered symptomatic relapse in the 9-month followup period, while only 17 percent of patients without a high EE relative relapsed.

As in the British studies, patients from high EE families who took neuroleptic medication regularly throughout the 9-month

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Table 1. The relationship of "expressed emotion" by key relatives to symptomatic relapse in schizophrenic patients

Study	Expressed emotion	Percent relapse 9 months[1]	Level of significance
Maudsley-London (Brown, Birley, and Wing 1972) $n = 101$	High Low	58 16	$p < .001$
Maudsley-London (Vaughn and Leff 1976) $n = 37$	High Low	48 16	$p < .001$
UCLA-Camarillo MHCRC $n = 54$	High Low	56 17	$p < .006$
UCLA-Camarillo MHCRC[2] $n = 36$	High Low	60 9	$p < .0046$

[1] A 2-year followup was also completed with the Vaughn and Leff sample with similar results.

[2] Those patients in the sample of 54 who lived with key relatives continuously during 9-month followup period.

followup period relapsed at a significantly lower rate than those who did not take medication regularly. In the low EE group there was no statistically significant difference in rates of relapse between the subgroups of patients who did and did not take regular medication.

There were some notable differences between the English and California subjects. In London, a majority of the families were rated low on EE, while in the California sample only one-third of the families were rated low on EE. Ratings of hostility were also significantly more common in the California families. Thus, while cultural differences may produce differing distributions of high vs. low EE in families containing a schizophrenic member, the pattern of high EE retains its predictive importance cross-culturally. It was also noted that many more of the California schizophrenic patients sustained high levels of schizophrenic symptoms continuously from the time of admission, through discharge, and to the 9-month followup point. Since these patients were at a ceiling level for schizophrenic symptoms, they were not included in the analysis. Continued followup is being carried out to ascertain patients' psychiatric status at 2 years postdischarge and its relationship to EE.

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Vaughn, C.E., and Leff, J.P. The influence of family and social factors in the course of psychiatric illness. *British Journal of Psychiatry*, 129:125–137, 1976.

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The **Psychosocial Rehabilitation Journal** is now under the joint sponsorship of the International Association of Psychosocial Rehabilitation Services (IAPSRS) and Boston University's Sargent College of Allied Health Professions, Department of Rehabilitation Counseling. The Co-Editors of the Journal are William Anthony, Center for Rehabilitation Research and Training in Mental Health, Boston University, and Julius Lanoil, College of Medicine and Dentistry, New Jersey Medical School. The Managing Editor is LeRoy Spaniol, Center for Rehabilitation Research and Training in Mental Health, Boston University.

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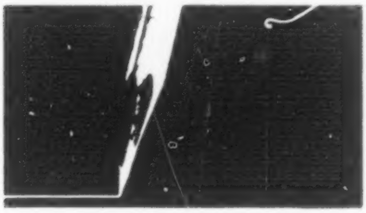

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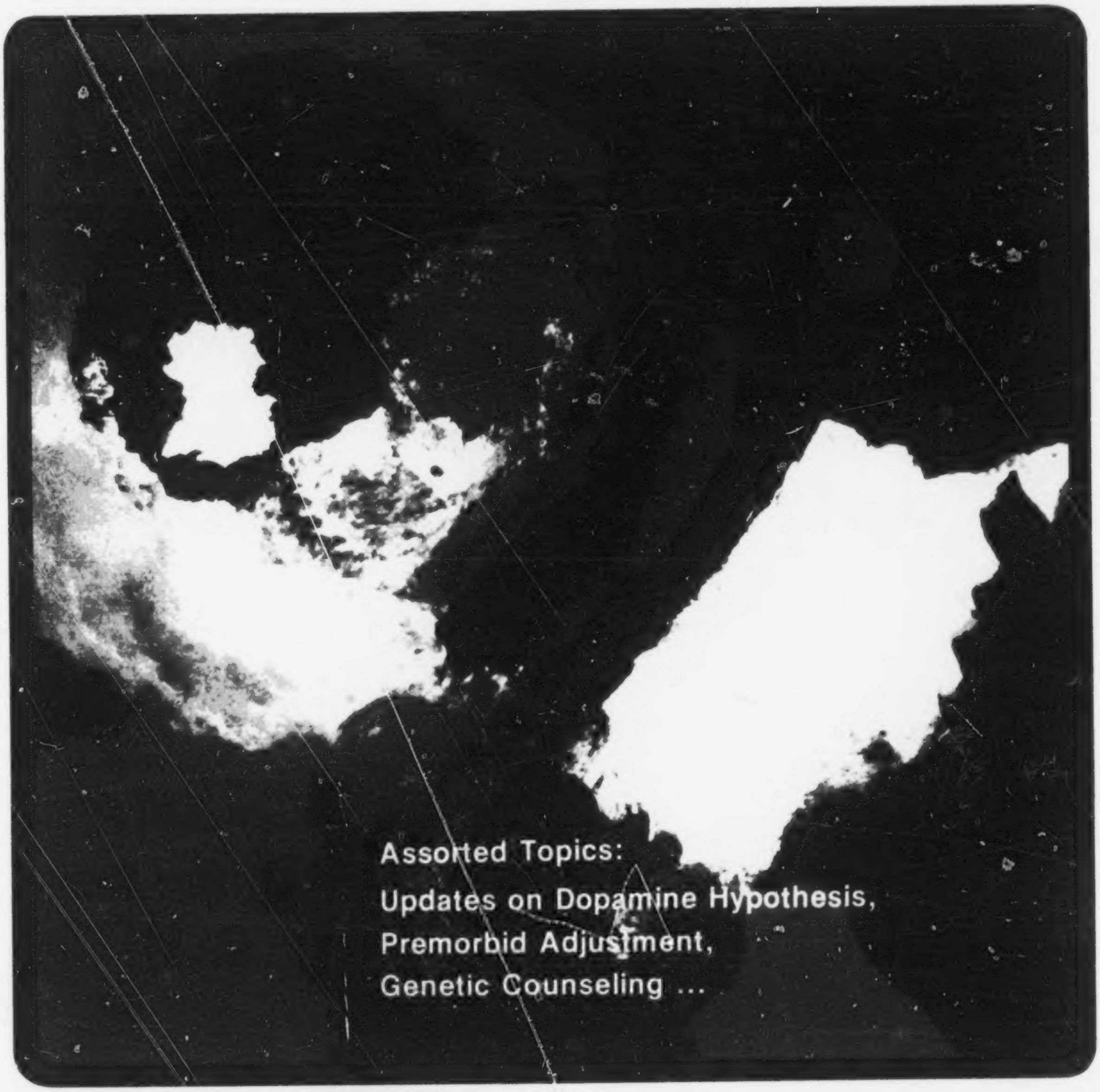

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About the Cover

The *Schizophrenia Bulletin* features art done by current and former mental hospital patients. The painting that appears on the cover of this issue was sent to us by Patricia Musick, Ph.D., A.T.R., Associate Professor, University of Houston at Clear Lake City, Houston, TX. The artist, who wishes to remain anonymous, has given permission to reproduce his painting in the *Bulletin*. Dr. Musick has provided the following description of the artist's work:

The interference theory of schizophrenia suggests that the dominant characteristic of such art is fragmentation, and that this is caused by the inability to maintain a perceptual set. Interference causes the artist to stereotype by repeating similar forms contiguously. Although the art work of this individual demonstrates such repetitions, the whole gestalt is one that provides aesthetic pleasure and the excitement of viewing unknown dimensions.

Identifying Schizophrenic Patients Who Should Not Receive Medication

by Peter Buckley

At Issue

Abstract

There is clinical research evidence that there exists a subgroup of schizophrenic patients who should not be treated with neuroleptics. To date there has been no reliable method of identifying these patients. Systematic predictive studies of different subjective experiences of schizophrenia are suggested as a method of elucidating who should or should not receive medication. The studies should focus on patients' psychological experience and attitude toward the illness both during the acute phase and recovery from psychosis and examine their relationship to clinical outcome. Such studies may have utility in developing psychological "markers" for treatment of subtypes.

For some time it has been apparent that there is a subgroup of schizophrenic patients who should not be treated with neuroleptics. Davis (1975), in a review of maintenance drug therapy in schizophrenia, has suggested that there is a population of patients who are quite different from patients with chronic relapsing schizophrenia and for whom maintenance drug therapy may not be indicated. Carpenter, McGlashan, and Strauss (1977) demonstrated that not using neuroleptics during an acute psychotic episode does not necessarily result in a disadvantageous course and outcome. The clinical outcome of a treatment program sharply limiting the use of medication and emphasizing psychosocial modalities for 49 acute schizophrenic patients was contrasted with that of 73 similar patients receiving standard treatment where the use of neuroleptics was ubiquitous. A followup at 1 year demonstrated a small, but significantly superior, outcome for the first group. Goldstein (1970), in a study of 54 newly admitted male schizophrenic patients treated with a fixed dosage of thioridazine or placebo over a 21-day period, found that good premorbid, nonparanoid schizophrenics showed no deterioration on placebo and little positive drug response, a finding suggesting that this group might be adversely affected by medication. In a study of acute schizophrenic patients randomly assigned to chlorpromazine or placebo, Rappaport, Hopkins, and Hall (1978) described a subgroup of patients who did better without medication.

To date there has been no reliable method of differentiating the schizophrenic patients who should not receive neuroleptics from those for whom such treatment is indicated. Given the incidence of serious side effects from neuroleptic medication, such a differentiation is of pressing clinical importance. Rappaport, Hopkins, and Hall (1978) also contend that, for some patients, medication negatively affects long-term adjustment.

Refinements in the clinical diagnosis of schizophrenia have done little to mitigate this problem, perhaps because of the virtual dearth of knowledge concerning the etiology of the schizophrenias, the absence of established biological

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markers, and the consequent diagnostic necessity of emphasizing phenomenology which is probably held in common by a heterogeneous group of disorders. Carpenter et al. (1978) have pointed out the surprising lack of relationship between various diagnostic systems and outcome in schizophrenia. They have demonstrated that past social functioning predicts future social functioning, past work performance predicts future work performance, but that the diagnosis of schizophrenia based on cross-sectional symptom criteria alone is of little value in predicting course and outcome and, consequently, in deciding who should or should not receive medication.

Subjective Experience as a Possible Discriminator of Treatment Subtypes

The traditional signs and symptoms of schizophrenia have been shown to be only weakly predictive of outcome. As a consequence, standard diagnostic criteria are unlikely to be helpful in identifying patients who would do well without medication. This being the case, what other diagnostic approaches might be tried? Focusing more closely on the psychological experience of the patient both during the acute phase and during recovery from a schizophrenic episode might prove to be fruitful. Freedman (1974) has previously suggested that closer study of the subjective experience of schizophrenia might be useful in differentiating subtypes of schizophrenia and pointed out that little empirical data exist on the inner experience of the "average" schizophrenic.

Numerous autobiographical accounts by schizophrenic patients have described changes in perception and cognition which are not normally emphasized in our current diagnostic frameworks (Freedman 1974). These subjective phenomena have also been described in other more benign altered states of consciousness such as religious conversion and psychedelic drug use (Bowers and Freedman 1966), and their presence in a schizophrenic episode might be indicative of a better prognosis. Such phenomena would include the presence of heightening or dampening of sensory awareness, changes in the perception of the passage of time, and the presence of an increased susceptibility to distraction by external stimuli. Whether patients are aware of an alteration of their normal means of experiencing themselves and the external world could also be formally assessed. The phenomenological overlap in some aspects of the acute mystical experience and acute schizophrenia (Buckley 1981) and the circumscribed, self-limited nature of the altered state of consciousness in the former suggest that the presence of similar subjective phenomena in some acute schizophrenics might be a possible marker of patients who should not receive medication. The study of such phenomena would, like other diagnostic efforts, be a phenomenological approach, but it would focus on perceptual and cognitive components of the psychotic experience that have not been studied for their usefulness in predicting outcome with and without medication.

Melges and associates (Melges and Fougerousse 1966; Melges et al. 1974; Melges and Freeman 1977) have found a significant positive correlation between temporal disorganization (racing of thoughts, confusion of sequences, and timelessness) and inner-outer confusion in both tetrahydrocannabinol intoxication and acute psychoses. In these studies, temporal disorganization was found to occur before the onset of symptoms of inner-outer confusion. Because temporal disorganization was related to problems with immediate memory, Melges and Freeman (1977) have suggested that treatments aimed at enhancing immediate memory might prove corrective. Patients who exhibit this phenomenon might be treated by psychotherapeutic strategies that would help them differentiate the present from the past and future and thus possibly correct their experiences of inner-outer confusion. It is conceivable that subjective experiences of racing of thoughts, confusion of sequences, and timelessness are "markers" of schizophrenic patients for whom a psychotherapeutic approach might be preferable to, or as potent as, a pharmacological one.

On a more complex level of subjective experience, the patient's interpretation of the psychotic episode as meaningful or revelatory and offering the opportunity for personal psychological growth might be tested as another differentiating factor. Bowers (1974) has demonstrated that early psychotic experience can be examined and evaluated along a continuum of psychological conflict and desire for psychological growth and has suggested systematic predictive study using such a measure.

Integration or attempted integration versus sealing-over and denial in the recovery phase following an acute psychotic episode also warrants systematic investigation as a factor in the decision to use, or continue to use, medication. McGlashan, Levy, and Carpenter (1975) provided working definitions of these two distinct recovery styles. They contrasted patients who showed awareness of the continuity in their psychological life from before the psychotic experience, during the episode, and through recovery to those who sealed over and isolated the psychotic experience. The former group tend to want to understand the psychotic episode while the latter do not. Soskis and Bowers (1969) in a followup study found that those patients who had a positive, integrating attitude toward their illness had a better outcome than those who had a negative isolating attitude. While this capacity for integration may reflect ego strengths for which rating scales exist (Bellak, Hurvich, and Gediman 1973), the ability to use such capacities in personal understanding of a psychotic episode may not be reflected in ratings of ego strengths per se.

In a similar study to that of Soskis and Bowers (1969), McGlashan and Carpenter (1981) obtained a partial replication of their results. They found that the less negative schizophrenic patients were about their illness and future, the better their outcome. A very positive attitude was not associated with good outcome, but the absence of a negative attitude appeared critical. They point out that while a psychotic episode may catalyze ultimate psychological growth, it is basically a pathologic state and a failure of adaptation rather than a successful negotiation of conflict. Those patients with good outcome did not idealize their psychotic experience, but also did not reject it as irrelevant or unimportant. McGlashan and Carpenter (1981) characterize this attitude as "realistic"—neither overly positive nor overly negative. The causal relationship between attitude and outcome could not be answered by this study, however, since both were measured simultaneously. Hence, prospective studies are necessary to assess the predictive value of attitude toward illness. Those patients who are free of both a negative attitude toward their illness and a romantic idealization of the psychotic experience might be studied to see if they can be maintained free of medication. Their psychological coping mechanisms and self-observing capacities appear to be more resilient than those of other groups of schizophrenic patients, and these same psychological attributes may have an antipsychotic effect that obviates the use of medication.

Assessment of aspects of subjective experience could well be crucial to direct pharmacotherapy decision-making as well. As Van Putten et al. (1981) point out, the schizophrenic patient's subjective response to antipsychotic drugs has received little systematic investigation. In a study conducted by these investigators of 63 newly admitted schizophrenic patients who were given a test dose of thiothixene, an initial dysphoric response was a powerful predictor of both immediate and eventual drug refusal. They found that dysphoric responders experienced significantly more extrapyramidal symptoms following the test dose. Some of this group did have a good clinical outcome when treated with very low doses of medication. When the patients were kept drug-free for a 7- to 14-day observation period, a spontaneous remission of psychoses did not occur. Eliciting a subjective dysphoric response to neuroleptics may be one means of identifying patients who should be treated with very low doses of medication.

Just as neuroleptics may be deleterious for some schizophrenic patients, there is evidence that intensive psychosocial treatments may also exacerbate the illness and be "toxic" for some patients (Goldberg et al. 1977). Identifying this group, for whom intensive psychosocial treatment is contraindicated (at least until patients are asymptomatic), is another critical issue for clinical research and practice and one that might also be profitably examined from the viewpoint of the subjective experience of the patient during the psychotic episode.

The inner experience of schizophrenia has been a neglected area of research on outcome. Prospective study of different subjective experiences of schizophrenia such as those outlined above, during both the acute and recovery phases of psychosis, might help to elucidate who should or should not receive medication or intensive psychosocial treatment and might help to develop psychological "markers" for treatment subtypes.

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What Is Schizophrenia?

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One of the main questions related to schizophrenia is, naturally enough, what is it? Such a question may seem obvious, naive, impossible, or any combination of these. And certainly it is a bit demanding to expect that anyone could say what schizophrenia is in 1,000 words. On the other hand, we felt that it was worth the effort. We hope that presenting these brief discusssions on "what is schizophrenia" by persons who have worked extensively in the field will allow the reader to note areas of overlap and disagreement as well as variations in emphasis. Although no one may yet be able to provide the definitive answer, at least this collection of informed opinions may help clarify the major questions. The essays by Herbert Y. Meltzer and Robert Paul Liberman are the first in a series. Further collections of these statements will be presented in subsequent issues. Readers' responses and comments are cordially invited.—*J.S.S., M.B.B., and S.J.K.*

"What is" questions call for answers that provide Platonic forms, essences, hard edges which distinguish one category from another. An attempt to do this for schizophrenia, given our current state of knowledge, would have little likelihood of providing an answer that would endure for the following reasons: (1) the lack of one or more pathognomonic laboratory abnormalities; (2) the controversy concerning current diagnostic schemata; and (3) the lack of agreement over whether "poor" outcome, characterized by intellectual, social, and affective deterioration, should be a criterion for the diagnosis. These, as well as other factors, suggest that schizophrenia cannot be explicitly described in the same way that one could define rheumatoid arthritis or even manic-depressive illness.

Nevertheless, I do have a personal idea of what schizophrenia is that structures how I approach diagnostic evaluation, treatment, and research in schizophrenia. In my view, schizophrenia should be seen as a phenotype, a group of disorders of the central nervous system of diverse etiology which produce a broad range of clinical signs and symptoms that include various combinations of delusions, hallucinations, thought disorder, affective and volitional disturbances, loss of ego boundaries, ambivalence, intellectual deterioration, and personality aberrations. Although most schizophrenics will experience a gross psychotic episode at some time during their lives, family studies suggest that some schizotypal individuals will prove to be part of the continuum of the organic brain disorders that comprise schizophrenia. I do not believe poor outcome is inevitable in schizophrenia, although, unfortunately, the majority of schizophrenic patients do have persistent psychotic symptoms as well as severe deficits in intellectual and affective capacities and work and social relationships.

We are, as yet, uncertain of the nature of the various types of central nervous system dysfunction which underlie schizophrenia. Abnormalities of the following types have been implicated: neurotransmitters such as dopamine, serotonin, or norepinephrine; neuropeptides such as β-endorphin, des-tyr-γ-endorphin, cholecystokinin; slow or standard viral infections; autoimmune processes; methylation of membrane phospholipids; prostaglandins—to name but the most currently interesting possibilities. One, more than one, or none of these may be involved. Some of these abnormalities may be based on genetic predispositions, acquired abnormalities, or both. If any of these, or similar hypotheses, are correct, then schizophrenia would clearly be an organic brain disease, albeit one with minimal structural changes identifiable at the microscopic level, at least with current techniques. As any type of central nervous system abnormality which produces one of the variants of schizophrenic psychopathology is identified, I suspect there will be a strong impulse to remove such cases from the category, just as has been the practice for schizophreniform psychoses which have been found to be due, for example, to Huntington's chorea, porphyria, or brain tumors. The remaining as yet unexplained psychoses would be considered schizophrenia. Schizophrenia would then be defined as those schizophreniform psychoses whose cause has not yet been ascertained. In the millenia, with all the causes fully catalogued, schizophrenia would cease to exist!

A second alternative, only slightly less appealing, would be to consider *all* cases with one of the schizophrenia phenotypes as schizophrenia, regardless of what central nervous system abnormality has been identified as the cause. This would even include brain tumors, birth trauma, trauma of later life, toxic psychoses, and known genetic disorders such as Huntington's chorea and porphyria. Clearly, schizophrenia would be a secondary diagnosis in such cases, but it would still be clinically important. For example, it would provide a picture of some aspects of the mental status and the clinical course, offer a guideline to certain types of treatment, and possibly sharpen prognostic implications.

A third alternative would be to limit schizophrenia to only a select group of central nervous system abnormalities producing schizophreniform psychoses, perhaps those without gross brain lesions and diffuse metabolic abnormalities, but including those with specific neurotransmitter, neuromodulator, or receptor abnormalities. This broad view of what is schizophrenia is not meant to diminish the need to identify the separate causes and pathophysiologies of the various subtypes of schizophrenia; rather, it is my intention to focus attention on the common elements, the final common pathways which converge to produce the schizophrenic phenotype, while we also identify its multiple etiologies.

It is clear that I disavow the notion of schizophrenia as a single disorder, but at the same time I do accept the Kraepelinean notion of distinguishing schizophrenia from the affective psychoses with their distinctive phenotype and course (characterized by predominant disturbance of mood with or without delusions, hallucinations, thought disorder, and bizarre behavior) with the following major difference. From my earliest research with neuromuscular abnormalities in the psychoses (increased serum creatine kinase activity, neurogenic muscle atrophy, sprouting of subterminal motor nerves, and increased excitability of the H-reflex recovery curve), I have advocated the idea that there is a core biological dysfunction common to schizophrenia, the affective psychoses, and the paranoid state. Recent findings with eye-tracking abnormalities and enlarged ventricles, once thought to be unique to schizophrenia, are consistent with this concept. The specific form of the psychosis may be determined by unique genetic, developmental, and environmental factors, but a common abnormality may be a major factor in the triad of delusions, hallucinations, and thought disorder that characterizes these disorders. The interaction of various neurotransmitters, neuromodulators, and neural circuitry could modify the basic psychotic process to produce specific signs and symptoms so that one element of the triad may be absent while other elements are present.

This terrible disease of the young will yield many of its secrets to neuroscience in the next few decades if the extraordinary flourishing of research begun in the 1960s and 1970s is not stifled by insufficient support. In the year 2000, an essay such as this might be able to discuss when in the developmental cycle specific genes and their products, in response to specific exogenous insults or stresses, produced various biochemical and electrophysiological abnormalities that, in turn, were the basis for specific abnormal behaviors in the numerous subtypes of schizophrenia. What a joy it will be to read, what an even greater joy to write, such an essay.

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> The patient asked his psychiatrist, "What is schizophrenia?" The psychiatrist replied, "Why do you want to know?" "Because if I've got it, I don't like it, and I'd like to get rid of it," responded the patient.

The mental gymnastics required to write a 1,000-word essay on the nature of schizophrenia are enough to provoke a thought disorder. It is indeed a challenge to go beyond the cherished litany of characteristic symptoms that comprise the clinical picture of schizophrenia, and the stress-diathesis model of its causation and course. Nonetheless, the challenge is captivating, and I will offer two propositions about schizophrenia that I hope will provoke thought and action about prevention and treatment.

1. **There are no schizophrenics.** Some persons experience delusions, hallucinations, incoherence, and associated social and behavioral impairments, but a person is generally not schizophrenic 24 hours a day. Some, more than others, must cope with varying degrees of cognitive distortions, psychophysiological arousal, information overload, and thought disorder. But the vulnerability to and symptoms of schizophrenia are marked more by variability than by constancy over time and across individuals.

Vulnerability to developing schizophrenic symptoms appears to reside in most people, given sufficient environmental stressors. When "normals" are asked to free associate without reference to the content of their speech, something similar to schizophrenic incoherence occurs. Soldiers with good premorbid adjustments have schizophrenic-like episodes if exposed to intense and prolonged combat. Furthermore, attempts to demonstrate discontinuities in prognoses of patients diagnosed as suffering from schizophrenic vs. affective disorders have revealed, not bimodal distributions, but rather linear outcomes on a continuum.

The biological bases for schizophrenia also show continuity between this disorder and other psychiatric disturbances. Genetic studies, for example, suggest that probands suffering with schizophrenic symptoms also have a disproportionate number of relatives with psychiatric disorders other than schizophrenia. The neuroleptic drugs are not specific to schizophrenic symptoms, but rather appear to possess broad, antipsychotic properties. Many of the presumptive biochemical markers for schizophrenia are, in fact, found in a wide range of psychotic disorders.

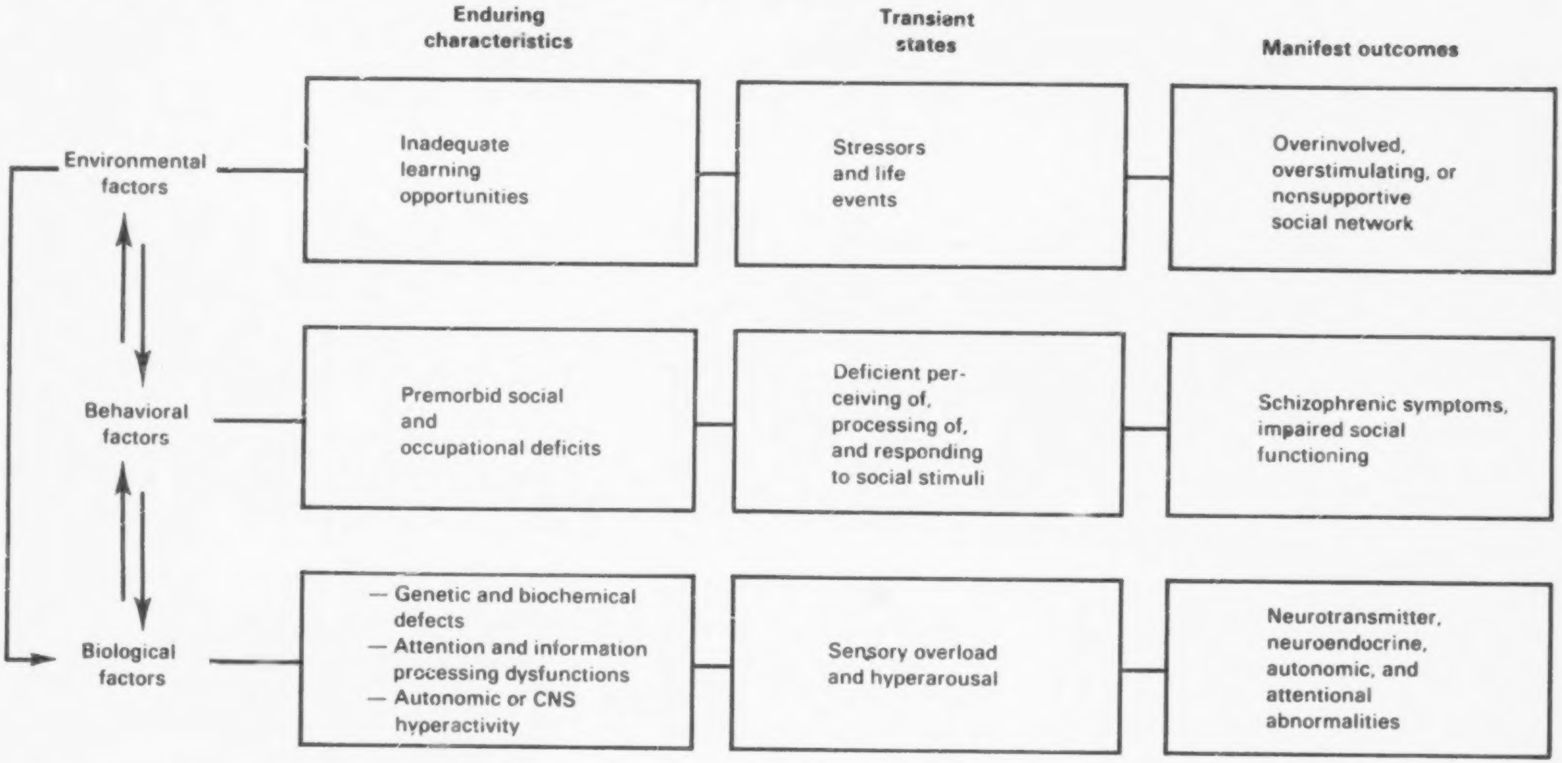
Although promising cognitive and psychophysiological markers for the underlying biological vulnerability to schizophrenic symptoms are being investigated, there is no evidence that such potential markers are discontinuous or dichotomous in their manifestations. In summary, intraindividual and interindividual variability are such visible features of the disorder that they should govern our conceptualization of the nature of schizophrenia.

Variability and continuity in the manifestation of the disorder suggest that the nature of schizophrenia is to be found in the *interactions* among behavior, environment, and biology. The causes, remissions, relapses, and idiosyncratic manifestations of symptoms and impairments in schizophrenia might best be discovered by methods that reveal the many faceted relationships among the individual's multimodal behavior, the biological matrix, and the environment. The multiplicity of environmental stressors, reinforcers, and supports; the probabilistic and plastic events within the central nervous system; and the ephemeral and dynamic modes of experience and behavior all promote the heterogeneity that emerges as the fundamental fact of schizophrenia. As figure 1 suggests, the nature of schizophrenia is to be found in the interactions and interfaces, and not in the person.

As we learn more about the specific variables involved in the interactions (e.g., the role of "expressed emotion" of relatives in the relapse of unmedicated patients), specific interventions can be designed for therapeutic benefit and prevention.

2. **Individuals with schizophrenic symptoms actively contribute to the development and course of their disorders.** Instead of viewing the pathogenesis of schizophrenia as arising mechanistically from biological and environmental determinants, it is useful also to see individuals as producers of their own development. Determinism of the onset and course of schizophrenia is reciprocal between the actions of the individual and the influences of past and current environments. The individual can affect his or her disorder through making choices

Figure 1. An interactional model for understanding the nature of schizophrenia


Enduring characteristics
Transient states
Manifest outcomes
Environmental factors
Behavioral factors
Biological factors
Inadequate learning opportunities
Stressors and life events
Overinvolved, overstimulating, or nonsupportive social network
Premorbid social and occupational deficits
Deficient perceiving of, processing of, and responding to social stimuli
Schizophrenic symptoms, impaired social functioning
— Genetic and biochemical defects
— Attention and information processing dysfunctions
— Autonomic or CNS hyperactivity
Sensory overload and hyperarousal
Neurotransmitter, neuroendocrine, autonomic, and attentional abnormalities

and exercising behavioral competencies or deficits that have impacts on the "world outside" (social environment) and the "world inside" (biological matrix). For example, a person with good social skills can solidify a social support network that, in turn, will aid in coping efforts, community survival, and problem solving. Such successful mastery experiences may also favorably affect neurotransmitters or other aspects of central nervous system function.

Before the onset of the disorder and thereafter, the individual is presented with an enormous range of possibilities for action or inaction. Thus, the conception of our patients as changing as they actively select from among innumerable environmental and behavioral possibilities replaces the conception of them as completely determined by structure and circumstances.

While theoretically free to choose their own course and personal trajectories, persons with schizophrenic vulnerability have a reduced capacity to act effectively in behalf of their own development because of impaired social perception, cognitive processing, and social competence. For example, the ability to generate alternative strategies for coping with problems in living and to anticipate their consequences is constricted. This means that the range of personal choices is down and that individuals are less likely to adapt successfully to and to affect their life space.

What can be done to improve vulnerable individuals' contributions to their life span development? Social skills training methods can increase the "receiving" and "information processing" skills of our patients and can widen their response competencies. To the extent that greater cognitive, social, and problem-solving skills are present, individuals may be better able to meet developmental potentials, generate social support, and reduce vulnerability. Of course, appropriate drug treatment, family intervention, environmental modification, and support services will also reduce vulnerability, improve the climate for learning skills, and maintain the skills that are acquired.

The aim of rehabilitation is not to cure disease, but to enhance a deficient individual's functioning, level of adaptation, and quality of life. The necessary design and validation of technology for skills training will include tools from psychopharmacology, social and cognitive psychology, psychodynamics, and social learning theory. For example, we already know that patients learn social problem-solving skills better when they are taking optimal doses of neuroleptics; when their relatives are involved in educational activities aimed at improving the family emotional climate; when they are exposed to repeated practice with slow and gradual steps, when visual as well as auditory cues and instructions are used; when positive feedback is liberally provided; when social modeling is provided that uses peers as well as therapists; and when skills training is personalized.

The further development of a technology for social and living skills training will also help us refine our knowledge of how different modalities of behavior interreact in persons vulnerable to schizophrenic symptoms. Does the affective modality, with its control of motivation, drive, and stimulus seeking, have primacy over cognitions and instrumental role behavior? Is it, as we suspect, necessary to bring symptoms under control before training social skills? Can we reduce relapse of symptoms by strengthening social competence?

As we increase the specificity of our assessment and intervention techniques, improve our understanding of the temporal phases of change across behavioral modalities, and the variability among individuals, we shall be better able to answer the question, "What is schizophrenia?"

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The Dopamine Hypothesis: An Overview of Studies With Schizophrenic Patients

by John L. Haracz

Abstract

For the past decade, the dopamine hypothesis of schizophrenia has been the predominant biochemical theory of schizophrenia. Despite the extensive study of tissue samples obtained from schizophrenics, indirect pharmacological evidence still provides the major support for the hypothesis. Direct support is either uncompelling or has not been widely replicated. The dopamine hypothesis is limited in theoretical scope and in the range of schizophrenic patients to which it applies. No comprehensive biological scheme has yet been proposed to draw together the genetic, environmental, and clinical features of schizophrenia. Recent refinements of the dopamine hypothesis may aid in the delineation of biologically homogeneous subgroups. Positive symptoms (e.g., hallucinations, delusions) and negative symptomatology (e.g., affective flattening, social withdrawal) may result from different pathophysiological processes. Schizophrenia research might benefit from an increased attention to neurophysiological adaptations.

The dopamine (DA) hypothesis of schizophrenia was founded on indirect pharmacological evidence. Early observations suggested a dopaminergic hyperactivity in schizophrenia: the symptoms of acute paranoid schizophrenia resemble the psychosis induced in nonschizophrenics by amphetamine, an indirect DA agonist (Young and Scoville 1938; Connell 1958; Bell 1965; Angrist et al. 1974); DA agonists exacerbate schizophrenic symptoms (Yaryura-Tobias, Diamond, and Merlis 1970; Janowsky et al. 1973; Angrist and Gershon 1977); a therapeutic effect is produced by drugs that block central dopaminergic transmission (Carlsson and Lindqvist 1963; Randrup and Munkvad 1972; Matthysse 1973). More recently, additional pharmacological support for the DA hypothesis has been generated by clinical and preclinical studies of numerous neuroleptic compounds. The clinical antipsychotic potencies of the neuroleptics were closely correlated with various measures of their antidopaminergic potency, such as the *in vitro* inhibition of DA receptor binding (Creese, Burt, and Snyder 1976; Seeman et al. 1976; Peroutka and Snyder 1980), the reversal of animal behaviors induced by DA agonists (Creese, Burt, and Snyder 1976), the elevation of human plasma prolactin levels (Langer et al. 1977), and inhibition of the electrically stimulated release of DA from brain slices (Seeman and Lee 1975).

The pharmacological support of the DA hypothesis has motivated a search for confirmatory evidence with the use of schizophrenic subjects. Several extensive reviews of the preclinical pharmacological evidence have appeared elsewhere (Matthysse 1974; Snyder et al. 1974; Meltzer and Stahl 1976; Carlsson 1978; Hornykiewicz 1978). The present article will review the biological studies that constitute direct and indirect tests of the DA hypothesis with schizophrenic subjects. Experimental reports will be organized into three

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groups according to the aspect of dopaminergic activity under study: (1) presynaptic dopaminergic mechanisms, (2) DA receptor sensitivity, and (3) the clinical effects of drugs that alter dopaminergic activity.

Presynaptic Dopaminergic Mechanisms

Post-mortem Brain DA and Homovanillic Acid (HVA). Several groups have tested the DA hypothesis by examining post-mortem brain levels of DA and its major metabolite, HVA, in schizophrenics and controls. DOPAC (3,4-dihydroxyphenylacetic acid), an intermediate in the formation of HVA, has also been measured. The literature contains some reports of altered DA and HVA levels in the brains of schizophrenics, but these results have not been widely replicated (table 1).

Farley and coworkers obtained post-mortem brain samples from 4 chronic paranoid schizophrenics and 12 controls with no history of neurologic or psychiatric illness (Farley, Price, and Hornykiewicz 1977; Farley, Shannak, and Hornykiewicz 1980). DA and HVA concentrations did not differ between schizophrenics and controls in the caudate, nucleus accumbens, putamen, and medial or lateral olfactory areas (table 1). Significantly elevated DA, but not HVA, was found in the ventral septum of the schizophrenics.

Crow et al. (1978, 1980) determined DA and HVA levels in the post-mortem brains of 19 general hospital controls and 19 chronic schizophrenics who were diagnosed according to Feighner's criteria (Feighner et al. 1972). They reported no differences between the groups in the nucleus accumbens and putamen (table 1). In the caudate, the schizophrenics had significantly elevated DA and decreased HVA concentrations compared to controls. There were no differences in DOPAC concentrations in any of the areas. As will be discussed later, elevated numbers of DA receptors were also found in caudate samples from the same patients (Crow et al. 1978; Owen et al. 1978). In post-mortem specimens from 9 chronic schizophrenics and 10 general hospital controls, Crow et al. (1979) later found significantly elevated DA in the caudate and putamen of the schizophrenics (table 1). Regional HVA and DOPAC did not differ between the groups.

Bird et al. (1977) measured DA concentrations in post-mortem brain samples from more than 50 controls, obtained from a general hospital, and a similar number of psychotic patients. The psychotic group was subdivided into "schizophrenia" and "schizophrenia-like" categories according to Schneiderian first-rank phenomena and chronicity of illness (Mackay et al. 1980a). The overall group of psychotics had significantly elevated DA levels in the nucleus accumbens and anterior

Table 1. DA and HVA levels in post-mortem brains of schizophrenics and controls

	Caudate		Nucleus accumbens		Putamen		Cingulate gyrus		Frontal lobe		Septal region	
Study	DA	HVA	DA	HVA	DA	HVA	DA	HVA	DA	HVA	DA	HVA
Farley, Shannak, and Hornykiewicz (1980)	N	N	N	N	N	N	—	—	—	—	↑	N
Crow et al. (1978, 1980)	↑	↓	N	N	N	N	—	—	—	—	—	—
Crow et al. (1979)	↑	N	N	N	↑	N	—	—	—	—	—	—
Bird et al. (1977)	N	—	↑	—	N	—	—	—	—	—	N	—
Bacopoulos et al. (1979)	—	—	—	N	—	N	—	↑	—	↑	—	—
Winblad et al. (1979)	N	N	—	—	N	N	N	—	N	—	—	—
Wyatt et al. (1981)	—	—	N	N	—	—	—	—	—	—	—	—

Note: ↑, ↓ = significantly increased or decreased in schizophrenics compared to controls ($p < .05$); N = no significant difference between schizophrenics and controls ($p > .05$); — = levels not reported. An effort was made to identify unique subject groups.

perforated substance, but there were no abnormal findings in putamen, caudate, septal nuclei, and amygdala central nucleus (Bird et al. 1977; Bird, Spokes, and Iversen 1979*a*, 1979*b*, 1980). The "schizophrenia" subgroup was itself subdivided into groups of patients who were over or under 25 years of age. Only the under-25 group of schizophrenics had significantly increased DA in the caudate and nucleus accumbens compared to controls (Mackay et al. 1980*a*). All but three of the schizophrenics in this study received chronic neuroleptic treatment before death.

Bacopoulos et al. (1979) determined post-mortem HVA levels in the brains of 25 schizophrenics who had received neuroleptics for periods ranging from 6 months to 17 years before death. Compared to age-matched controls, the schizophrenics had significantly elevated HVA in the cingulate gyrus, temporal lobe, and orbital frontal cortex, but there were no differences in the nucleus accumbens or putamen (Bacopoulos et al. 1979; Bacopoulos, Bird, and Roth 1979). Levels in the caudate nucleus were not reported. HVA concentrations were within the control range in three schizophrenics who apparently had not been treated with neuroleptics. It was proposed that the elevated HVA in the cortical regions indicated a lack of tolerance to the neuroleptic effects in these areas, possibly suggesting a cortical site of antipsychotic action.

Winblad et al. (1979) recently measured post-mortem concentrations of DA and HVA in the brains of 28 nonpsychiatric controls and 12 schizophrenics, 6 of whom had been "lobotomized" 25 to 30 years before death. All the schizophrenic patients had been on neuroleptics and were diagnosed according to Bleulerian criteria. There were no significant differences between controls and schizophrenics in the DA concentrations of caudate, putamen, hypothalamus, thalamus, mesencephalon, pons, hippocampus, frontal lobe, and the cingulate gyrus (table 1). HVA levels did not significantly differ between the groups in the caudate and putamen.

Finally, the concentrations of DA and its metabolites were determined by Kleinman and coworkers in post-mortem brain specimens from 17 normals and 32 psychiatric patients (Kleinman et al. 1980; Wyatt et al. 1981). Psychiatric diagnoses fell into the following groups using Research Diagnostic Criteria (Spitzer, Endicott, and Robins 1975): chronic undifferentiated schizophrenia ($n = 11$), chronic paranoid schizophrenia ($n = 11$), and other psychiatric disorders ($n = 10$). No significant differences for DA, DOPAC, or HVA were found in either the nucleus accumbens or the hypothalamus of any of the patient groups relative to controls.

Since the majority of the schizophrenics in the above studies received neuroleptics shortly before death, drug effects must be considered in the interpretation of the positive findings. Drug-free schizophrenics and controls were reported to have similar DA and HVA concentrations in several brain regions (Bacopoulos et al. 1979; Kleinman et al. 1980). Preliminary studies indicated that schizophrenics and nonschizophrenics did not differ in the post-mortem fluorescence histochemistry of catecholamine neurons in cortical and subcortical regions (Olson, Nystrom, and Seiger 1973*a*, 1973*b*; Olson 1974). These findings do not support the presence of elevated DA turnover in the brains of schizophrenics.

Cerebrospinal Fluid (CSF) HVA. CSF HVA measurements have been used to estimate the activity of central dopaminergic neurons (Bowers 1972; Sourkes 1973). The nigrostriatal DA system appears to be the major source of CSF HVA (Sourkes 1973). The mesolimbic and mesocortical DA tracts, which are more likely to be the etiologically important tracts in schizophrenia, probably make a relatively small contribution to CSF HVA (Meltzer and Stahl 1976). Until the central sources of HVA are better understood, it will be difficult to judge the meaning of CSF HVA findings in schizophrenia.

Bowers (1973) measured HVA and 5-hydroxyindoleacetic acid (5-HIAA), a serotonin metabolite, in CSF from 18 patients who were being treated for "acute psychotic reactions" included in the "schizophrenia spectrum." Neuroleptic treatment was withheld for 2 weeks before CSF sampling, and probenecid was administered to allow accumulation of the CSF metabolites. Two control groups consisted of unipolar depressive patients and healthy volunteer inmates. CSF levels of HVA, 5-HIAA, and the 5-HIAA/HVA ratio did not differ between schizophrenics and controls. When the schizophrenics were divided according to the presence or absence of Schneider's (1959) first-rank symptoms, the 5-HIAA/HVA ratio of the Schneider-positive group was significantly increased in comparison with the Schneider-negative patients, depressed patients, and inmates. The higher HVA concentration of the Schneider-negative group was just short of significance compared to the Schneider-positive group ($p < 0.1$). The Schneider-negative patients had significantly higher HVA levels than the inmate controls. CSF probenecid concentrations were not measured in any of the subjects, so a differential probenecid effect cannot be excluded as a cause of these findings.

Normal baseline HVA levels were found in the CSF of schizophrenics in studies that did not make use of probenecid (Chase, Schnur, and Gordon 1970; Fyrö et al. 1974; Sedvall et al. 1974). These patients had not received neuroleptics for at least 2 weeks.

Employing probenecid, two other laboratories also reported normal concentrations of CSF HVA in schizophrenics who were diagnosed according to Feighner's criteria (Post et al. 1975; Berger et al. 1980). Post et al. (1975) found no significant differences in baseline or postprobenecid CSF HVA levels between 25 drug-free acute schizophrenics and a control group consisting of normals and patients with neurological disorders or affective illness. In agreement with Bowers (1973), Post et al. reported that the schizophrenics with more first-rank symptoms had significantly lower postprobenecid HVA levels than a group of schizophrenics with few first-rank symptoms. HVA concentrations were not related to psychomotor excitement in Post's study, but CSF probenecid levels were not measured. Berger et al. (1980) reported no significant differences between normals and schizophrenics in baseline or postprobenecid CSF HVA and DOPAC levels. These patients were kept neuroleptic-free for 2 weeks and the results were statistically corrected for measured CSF probenecid concentrations. The postprobenecid CSF HVA levels found in 33 acute schizophrenics by van Praag (1977) were similar to the levels reported in schizophrenics in the above studies.

Bowers (1974) determined CSF probenecid and HVA levels in 17 patients who received a clinical diagnosis of "schizophrenic reaction." Neuroleptic treatment was stopped 2 weeks before study. The schizophrenics had significantly lower postprobenecid CSF HVA levels compared to 11 patients with bipolar affective disorder, exhibiting primarily mania. When the schizophrenics were divided according to their scores on the prognosis scale of Stephens and Astrup (1963), the poor prognosis group had significantly lower HVA concentrations than the better prognosis group. It was noted that the "paranoid psychotics" studied by Rimon et al. (1971) might have fitted into Bowers' better prognosis group of schizophrenics. Thus, a relationship between good prognosis and high CSF HVA might explain the finding reported by Rimon et al. of significantly higher baseline CSF HVA levels in a group consisting of paranoid schizophrenics and "other paranoid psychoses" compared to a control group of neurotics and affectively ill patients. Bowers (1974) found no differences in CSF probenecid concentrations among his groups, so the observed changes were apparently not due to a differential probenecid effect. He speculated that the relationship between poor prognosis and low CSF HVA may be due to a postsynaptic supersensitivity or to a substance other than DA that stimulates postsynaptic receptors, leading to a feedback inhibition of DA-releasing neurons (Bowers 1974, 1978).

Subsequently, Bowers' laboratory compared postprobenecid HVA concentrations between 10 patients with depressive illness and a group of 10 patients which included acute and chronic schizophrenics meeting Feighner's criteria (Kirstein, Bowers, and Heninger 1976). The schizophrenics had significantly higher CSF HVA levels than the depressed patients. HVA concentrations were unrelated to CSF probenecid levels or body movement in both schizophrenics and depressed controls. Thus, Bowers (1976) reports an overall pattern in which chronic schizophrenics tend to have lower CSF HVA values than manics, and acute schizophrenics have higher CSF HVA levels than depressed patients.

Most recently, Bowers and his coworkers assayed HVA, 5-HIAA, and probenecid levels in CSF from 30 young schizophrenics (mean age in years ± SD: males, 23.1 ± 2.8; females, 24.3 ± 7.8), 41 patients with major affective disorders (bipolar I, $n = 11$; bipolar II, $n = 4$; unipolar, $n = 26$), and 31 schizoaffective patients (Leckman, Bowers, and Sturges 1981). All of the subjects had been drug-free for 2 weeks and were diagnosed according to Research Diagnostic Criteria (Spitzer, Endicott, and Robins 1975). Ratings of premorbid sexual adjustment were completed for all subjects with an abbreviated form of the Phillips Rating Scale of Premorbid History (Harris 1975). Postprobenecid CSF HVA and 5-HIAA concentrations did not differ among the diagnostic groups. Within the group of schizophrenics, but not in the other diagnostic groups, poor premorbid sexual adjustment was associated with significantly higher CSF HVA levels and a high ratio of HVA concentration to log probenecid concentration. At first glance, this finding seems inconsistent with the previously reported correlation between poor prognosis and low CSF HVA among schizophrenics (Bowers 1974). The authors indicated, however, that a direct comparison between the studies is problematic since the Stephens-Astrup prognosis scale employed earlier contains only one item (out of 11) that relates to sexual functioning.

Sedvall and Wode-Helgodt (1980) measured baseline CSF monoamine metabolite levels in 36 hospitalized schizophrenics. Their patients met Research Diagnostic Criteria and had not received psychoactive drugs for 1 month before study. Eleven (30 percent) of the schizophrenics had a sibling, parent, aunt, or uncle with a diagnosis of schizophrenia. This group of patients with a family history of schizophrenia had significantly higher mean CSF levels of HVA and 5-HIAA, but not 3-methoxy-4-hydroxyphenylglycol (MHPG), compared to the schizophrenics without such a family history. The authors tentatively concluded that there is one group of schizophrenic disorders that has a disturbance in central DA and serotonin metabolism and a family disposition that may be genetically determined; another group of schizophrenic disorders has a normal central monoamine metabolism and no or a weak hereditary disposition.

In summary, the studies reviewed above have not shown differences in CSF HVA concentrations between schizophrenics and normal or neurological controls. One laboratory has found that the CSF HVA values of schizophrenics tend to lie above the values of depressed patients and below those in patients exhibiting mania (Bowers 1976). Independent investigators have reported that, in schizophrenic subjects, low CSF HVA is associated with poor prognosis (Bowers 1974) and the presence of first-rank symptoms (Bowers 1973; Post et al. 1975), whereas high CSF HVA is significantly related to a positive family history of schizophrenia (Sedvall and Wode-Helgodt 1980) and poor premorbid sexual adjustment (Leckman, Bowers, and Sturges 1981).

Enzyme Activities

Dopamine-β-hydroxylase (DBH). DBH activity in schizophrenics is of interest because it may relate to the DA hypothesis of schizophrenia as well as the hypothesis of Stein and Wise (1971) that noradrenergic "reward" pathways are damaged in schizophrenia. These investigators reported that their hypothesis was supported by a significantly decreased DBH activity in post-mortem specimens of hippocampus, diencephalon, and pons-medulla in 18 schizophrenics compared to 12 nonpsychiatric controls (Wise and Stein 1973; Wise, Baden, and Stein 1974). However, this finding has not been confirmed by later studies (Wyatt et al. 1975, 1978; Cross et al. 1978; Crow et al. 1979). Wyatt et al. (1975, 1978) found no significant differences in the DBH activities of post-mortem hypothalamus, hippocampus, and pons from nine chronic schizophrenics and nine nonpsychiatric controls. They suggested that:

> negative correlations between enzyme activity and both morgue-to-autopsy time and neuroleptic dose will explain at least some of the differences between schizophrenics and controls reported by Wise and Stein, as they appear to do in our data. [Wyatt et al. 1975, p. 369]

Another laboratory demonstrated closely similar DBH activities in 12 schizophrenics and 12 general hospital controls in post-mortem samples of hippocampus, hypothalamus, and four cortical areas (Cross et al. 1978; Crow et al. 1979). Lerner et al. (1978) reported no significant differences in CSF DBH activities among four diagnostic groups: schizophrenia or schizoaffective disorder ($n = 11$), major depressive disorders ($n = 16$), alcoholism ($n = 16$), and personality disorders ($n = 5$).

Several studies indicate that plasma DBH activity is not significantly different in schizophrenics and normal controls (Shopsin et al. 1972; Wetterberg et al. 1972; Dunner et al. 1973; Lamprecht et al. 1973; Meltzer et al. 1976; Meltzer, Nasr, and Tong 1980; DeLisi et al. 1980, 1981*a*). Taken together, these investigations compile data on 333 schizophrenics and 423 normals. Two studies actually found tendencies toward higher mean DBH activities in schizophrenics compared to controls: Markianos, Mystrom, and Reichel (1976) and Lamprecht et al. (1973), respectively, reported 38-percent and 35-percent increases in schizophrenics. Okada et al. (1976) reported that the 24-hour rhythm of plasma DBH activity in eight chronic schizophrenics was similar to that in normal subjects.

In contrast to the above findings, Fujita et al. (1978, 1979) reported a significant 59-percent decrease in plasma DBH activity in 159 schizophrenics compared to 153 normals. These patients met Schneider's (1959) diagnostic criteria and were receiving neuroleptics during the study. The report by DeLisi et al. (1981*a*) of a neuroleptic-induced 27-percent decrease in the plasma DBH activities in a group of schizophrenics suggests that at least some of the decrement observed by Fujita et al. (1978, 1979) may have been drug-induced. Alternatively, it has been speculated that the conflicting results of Fujita et al. (1978, 1979) may be due to differences in the presence and penetration of the DBH gene in the schizophrenic populations of different nationalities (Meltzer, Nasr, and Tong 1980).

Lamprecht et al. (1973) measured plasma DBH activity in 12 pairs of monozygotic twins discordant for schizophrenia. There was a highly significant correlation between enzyme activities in schizophrenic and nonschizophrenic cotwins, suggesting that plasma DBH activity is genetically determined. Baron, Levitt, and Perlman (1980) found that plasma DBH was significantly reduced in schizophrenics with a family history of schizophrenia spectrum disorders compared to a group of schizophrenics with unaffected relatives and a group of unrelated normal controls. Plasma DBH was also significantly lower in 9 schizophrenics compared to 26 of their normal relatives in an isolated Swedish pedigree (Böök, Wetterberg, and Modrzewska 1978; Wetterberg et al. 1979). However, DeLisi et al. (1980) reported that schizophrenic family members had higher plasma DBH activities than their healthy relatives in 9 of 13 American families ($p < .01$). Again, the apparent disagreement between these results might be secondary to international differences in some characteristics of the DBH gene.

All of the above results were obtained when DBH activity was assayed in the presence of Cu^{+2} and/or *N*-ethylmaleimide in order to antagonize endogenous DBH inhibitors. Most of the studies have found no evidence of a significant decrease in brain, CSF, and plasma DBH activity in schizophrenics. Accordingly, Yu et al. (1980) recently reported that plasma DBH activity, assayed with Cu^{+2} and *N*-ethylmaleimide, was not significantly different in 24 chronic schizophrenics compared to 20 normal controls. When the assay was conducted without anti-inhibitors, though, the "apparent" DBH activities were considerably reduced in all cases, with the schizophrenic group becoming significantly lower than the control group. The plasma of four of the schizophrenics induced a 30- to 70-percent inhibition of purified bovine DBH activity *in vitro*. The authors hypothesized that some schizophrenics have unusually high endogenous DBH-inhibitory activity or a deficiency in the copper cofactor. In this regard, Wise and Stein (1973) reported that dialysis of brain homogenates did not affect enzyme activity, suggesting that their finding of decreased brain DBH in schizophrenics was not due to an excess of endogenous dialyzable inhibitors. Wyatt et al. (1978) found no significant differences in DBH-inhibitory activity between chronic schizophrenics and controls in postmortem hypothalamus and hippocampus. Furthermore, several studies indicate that schizophrenics actually have elevated plasma copper levels (reviewed by Baron et al. 1982). The novel results of Yu et al. (1980) require further clarification, including the assay of plasma DBH-inhibitory activity in schizophrenics and controls.

Monoamine oxidase (MAO) and catechol-*O*-methyl transferase (COMT). A lowered activity of a DA-degrading enzyme in schizophrenics would have obvious relevance to the DA hypothesis. In a recent review, Wyatt et al. (1980) reported that 22 out of 32 studies found significantly lower platelet MAO activity in chronic schizophrenics compared to controls. Acute schizophrenia generally is not associated with low platelet MAO activity (Wyatt et al. 1980). Some studies indicate that decreased platelet MAO activity may be especially prevalent among schizophrenics with auditory hallucinations and paranoid features (Wyatt et al. 1980; Jeste et al. 1982). The importance of endogenous MAO inhibitors in the plasma of chronic schizophrenics has not been settled (Vogel, Ladman, and Berrettini 1980; Demisch et al. 1981). Significantly reduced MAO activity was also found in the lymphocytes of chronic schizophrenics (Sullivan et al. 1978), and in skeletal muscle from acute and chronic schizophrenics (Meltzer, Jackman, and Arora 1980). Acute, but not chronic, schizophrenics were reported to have significantly decreased plasma amine oxidase activity (Meltzer et al. 1980*a*).

The MAO findings outlined above have an unclear etiological significance, especially since: neuroleptics can reduce platelet MAO activity in schizophrenics (Friedhoff, Miller, and Weisenfreund 1978; Jackman and Meltzer 1980; Chojnacki et al. 1981; DeLisi et al. 1981*b*; Sahai, Arora, and Meltzer 1981); low platelet MAO activity is also present in many normals (Buchsbaum, Coursey, and Murphy 1976; Murphy et al. 1977); the greatest group mean reduction of activity observed by any study was only 68 percent in schizophrenics compared to controls (Wyatt et al. 1980). Moreover, brain MAO activity apparently is not decreased in schizophrenics. Seven recent post-mortem studies found no differences between controls and schizophrenics in the MAO activities of up to 14 brain areas, using a wide range of MAO substrates (Meltzer, Jackman, and Arora 1980; Reveley et al. 1981). It is possible that a decreased peripheral MAO activity is only one factor, among other genetic and environmental factors, contributing to the etiology of schizophrenia (Wyatt et al. 1980).

Wise, Baden, and Stein (1974) measured post-mortem COMT activity in the brains of 18 schizophrenics and 12 controls. They reported a significantly decreased activity in the diencephalon of the schizophrenics, with no difference in the pons-medulla. The authors cautioned that this deficit must be regarded as provisional until verified in larger populations because individual values of COMT varied widely in the schizophrenics. More recently, two laboratories reported no differences in post-mortem COMT activity between schizophrenics and controls in up to 14 brain regions, including the hypothalamus and thalamus (Cross et al. 1978; Wyatt et al. 1978; Crow et al. 1979).

Poitou, Assicot, and Bohuon (1974) found that membrane-bound, but not soluble, erythrocyte COMT activity was significantly increased in schizophrenics compared with normal controls. Matthysse and Baldessarini (1972) reported a slightly greater ($0.05 < p < 0.1$) whole blood COMT activity in 20 chronic schizophrenics compared to 13 nonschizophrenic psychiatric patients. Three other groups found no differences between schizophrenics and controls in soluble erythrocyte COMT activity (Dunner et al. 1971; Briggs and Briggs 1973; Ebstein et al. 1976). Shopsin et al. (1973) reported an increased K_m value for the soluble erythrocyte COMT in paranoid schizophrenics compared to either schizoaffective or chronic undifferentiated types.

Tyrosine hydroxylase (TOH) and dihydroxyphenylalanine decarboxylase (DD). Excessive DA synthesis conceivably could result from elevated activities of TOH and DD in dopaminergic neurons. One laboratory reported that the rate of decarboxylation of ^{14}C– labeled *dl*-dihydroxyphenylalanine (*dl*-DOPA) by erythrocytes was elevated in schizophrenics with hallucinations and thought disorder compared to normals and schizophrenics in remission (Tran, Laplante, and Lebel 1971; Tran-Manh et al. 1972). The authors concluded that this result may have been due to either an increased DD activity or an increased physical transport of DOPA across the cell membrane, or both. The functional importance of an elevated DD activity is uncertain since rat brain DD is normally present in great excess in comparison to TOH (Carlsson et al. 1972*a*). Thus, it seems improbable that an elevated DD activity alone could lead to excessive DA synthesis in schizophrenia. Furthermore, post-mortem brain DD and TOH activities did not significantly differ between schizophrenics and controls in the putamen, caudate, substantia nigra, and globus pallidus (Wyatt et al. 1978). Crow et al. (1979) also found that post-mortem TOH activity was similar in schizophrenics and controls in the putamen, caudate, and nucleus accumbens.

Urinary Metabolites. Urine specimens have not been a primary source of information about central biogenic amine metabolism in schizophrenia because of the contamination by peripheral metabolites in the sample (Goodwin and Post 1975). However, the urine may contain abnormal metabolite levels if schizophrenics have a functional deficit in the peripheral metabolism of biogenic amines (i.e., a decreased peripheral MAO activity). Elevated unmetabolized biogenic amines could then cross the blood-brain barrier to cause behavioral symptoms. With this reasoning in mind, it is interesting that four out of six studies have found evidence of elevated phenylethylamine (PEA) levels in the urine of some schizophrenics (Wyatt et al. 1980; Jeste et al. 1981). PEA structurally resembles amphetamine and is known to induce a hyperactivity syndrome in animals which resembles the effects of dopaminergic drugs (Potkin et al. 1979). Potkin et al. (1979) recently measured the 24-hour excretion of PEA in 32 normals and 31 chronic schizophrenics, 16 of whom had paranoid symptoms. The normals and nonparanoid patients did not differ in PEA excretion, but urinary PEA was significantly elevated in the paranoid group compared to controls. The paranoid and nonparanoid groups each had significantly decreased urinary phenylacetic acid (PAA) and elevated PEA/PAA ratios (Potkin, Wyatt, and Karoum 1980). These results suggest that some schizophrenics may have a functionally deficient activity of peripheral type B MAO, which converts PEA into its major metabolite, PAA (Domino 1980). It is noteworthy that PEA readily crosses the blood-brain barrier, and also has the highest affinity for type B MAO among the known endogenous substrates for the enzyme (Yang and Neff 1973; Domino 1980; Wyatt et al. 1980).

The existence of a type B MAO deficiency is also supported by the frequently observed peripheral MAO deficits in chronic schizophrenics (Wyatt et al. 1980). Peripheral MAO, such as in human platelets and skeletal muscle, is largely of the B type (Domino 1980). A functional type B deficiency might be expected to yield low levels of HVA in bodily fluids since DA is a mixed A and B MAO substrate that is largely converted to HVA (Goodall and Alton 1968; Domino 1980). However, Domino (1980) found no significant differences in urinary HVA levels between seven drug-free chronic schizophrenics and seven controls. Bowers (1976) suggested that a central type B MAO deficiency may be responsible for the low CSF HVA levels in chronic schizophrenics with poor prognoses. This hypothesis seems less likely in view of several recent reports that brain MAO activity is not reduced in schizophrenics (Meltzer, Jackman, and Arora 1980). Along this line, Reynolds et al. (1979) reported that CSF PAA levels were actually elevated in nine schizophrenics compared to controls. The latter finding casts further doubt on a central MAO deficiency and, instead, may reflect an abnormal elevation of PEA in schizophrenia.

Using the hypothesis that schizophrenics have a peripheral deficit in pure type B MAO, Domino (1980) predicted that the patients should have abnormal urinary levels of the substrates and products of type B, but not type A MAO. As expected, Domino (1980) found no evidence of a decreased type A MAO activity in chronic schizophrenics when he measured urinary levels of type A or mixed A and B MAO metabolites. It was proposed that a type B MAO functional deficiency could be tested for by examining the levels of type B substrates and their metabolites in the urine of schizophrenics under excess substrate conditions *in vivo* (Domino 1980).

DA Receptor Sensitivity

Post-mortem Brain Binding of DA Agonists and Antagonists. A recent theoretical trend has turned toward the consideration of postsynaptic receptor pathology since the majority of studies have not demonstrated an elevated DA turnover in schizophrenia (Bowers 1974; Snyder 1976). Four out of five laboratories have provided evidence for a postsynaptic dopaminergic supersensitivity in the post-mortem brains of schizophrenics (Lee et al. 1978; Owen et al. 1978; Mackay et al. 1980*a*, 1980*b*; Reisine et al. 1980*a*, 1980*b*; Reynolds et al. 1980, 1981).

Lee and Seeman (1980*a*, 1980*b*) have determined the specific binding of ^{3}H-neuroleptics in the postmortem brains of 59 neurologically normal controls and 50 schizophrenics who were diagnosed according to the presence of Schneider's first-rank symptoms. ^{3}H-Haloperidol and ^{3}H-spiperone binding was significantly elevated in the caudate and putamen of schizophrenics compared to controls, but ^{3}H-apomorphine binding did not differ between the groups in the same regions (Lee et al. 1978; Lee and Seeman 1980*a*, 1980*b*; Seeman et al. 1980). ^{3}H-Neuroleptic binding was also significantly increased in both the caudate and putamen of 11 schizophrenics who had no history of long-term neuroleptic treatment.

Owen et al. (1978) obtained post-mortem brain samples from 19 general hospital controls and 19 schizophrenics who met Feighner's diagnostic criteria. Compared to controls, the schizophrenics had significantly elevated ^{3}H-spiroperidol binding in the caudate, putamen, and nucleus accumbens. The binding of ^{3}H-ADTN, a DA agonist, did not differ between the groups in the caudate and putamen (Cross, Crow, and Owen 1979; Crow et al. 1980). Scatchard analysis of the spiroperidol binding in the caudate revealed a significantly increased number of receptors and a decreased receptor affinity in the schizophrenics. On the basis of animal experiments, the apparently reduced affinity was attributed to the presence of residual neuroleptics in the brain samples. Maximum spiroperidol binding was significantly increased but affinity was unchanged in the caudates of five patients who had no neuroleptic treatment for at least 1 year before death. These findings were recently confirmed by the Scatchard analysis of ^{3}H-flupenthixol binding in caudate samples from seven drug-free schizophrenics (Cross, Crow, and Owen 1981). The use of a selective DA D2 receptor antagonist indicated that only the D2, and not the D1, component of ^{3}H-flupenthixol binding was elevated in drug-free patients. Thus, it is suggested that schizophrenia is associated with a supersensitivity of the D2 type of DA receptor which is not linked to an adenylate cyclase.

The binding of ^{3}H-spiroperidol was determined by Reisine et al. (1980*a*, 1980*b*, 1980*c*) in the post-mortem brains of 11 nonneurological controls and 11 schizophrenics. In a comparison with controls, ^{3}H-spiroperidol binding was significantly increased in both the caudate and putamen of the schizophrenics, but was unaltered in the frontal cortex. Significantly elevated caudate binding was also found in three schizophrenics who were not receiving neuroleptic therapy at the time of death.

Mackay et al. (1978) reported a nonsignificant elevation of ^{3}H-spiperone binding in the nucleus accumbens of 26 schizophrenics compared to 17 controls. However, these investigators repeated the study and found that another group of schizophrenics had significantly increased numbers of receptors and a decreased receptor affinity in the caudate and nucleus accumbens (Mackay et al. 1980*a*, 1980*b*). In agreement with Owen et al. (1978), the authors felt that the decreased receptor affinity observed in schizophrenics was the result of competition for ^{3}H-spiperone binding by neuroleptic agents remaining in the brain after death. Mackay et al. (1980*b*) emphasized that the DA receptor alterations were not seen in a subgroup of schizophrenics who were free of neuroleptic drugs for 1 month or more before death. Compared to controls, both the receptor numbers and affinities were not significantly different in samples of caudate from seven drug-free patients and nucleus accumbens from four drug-free patients. This result differs from previous reports of elevated brain ^{3}H-neuroleptic binding in drug-free schizophrenics by Lee and Seeman (1980*a*, 1980*b*; drug-free $n = 11$); Cross, Crow, and Owen (1981; $n = 7$); and Reisine et al. (1980*a*, 1980*b*; $n = 3$).

In contrast to the results of the four laboratories reviewed above, Reynolds et al. (1980, 1981) found that the post-mortem putamen binding of ^{3}H-spiperone did not differ between 17 nonpsychiatric controls and 10 schizophrenics meeting Feighner's diagnostic criteria. The receptor numbers of four drug-free schizophrenics tended to lie within the control range (Reynolds et al. 1980). In accord with Owen et al. (1978) and Mackay et al. (1980*b*), receptor affinities were lower in neuroleptic-treated schizophrenics as compared to either the controls or drug-free patients (Reynolds et al. 1980).

More work is needed to determine whether the elevated brain binding of ^{3}H-neuroleptics, reported by four out of five laboratories, is secondary to a drug effect or to the schizophrenic disease process. Animal investigations indicate that chronic neuroleptic treatment induces a postsynaptic DA receptor supersensitivity (Muller and Seeman 1978; Haracz and Tseng 1980). The schizophrenia binding studies have included only a small number of patients who were drug-free for 1 month or more before death. As pointed out above, there is conflicting evidence as to the presence of DA receptor abnormalities in drug-free schizophrenics.

Further clarification may be obtained by comparing the characteristics of DA receptors in brain samples from neuroleptic-treated animals and recently deceased schizophrenics. Already, Crow (1980) has underscored some differences in the animal and human data that may suggest that the schizophrenia binding results are not drug-related. Chronic neuroleptic administration to animals induced a smaller elevation in receptor number than that seen in many schizophrenics. Moreover, only the type of receptor labeled by DA antagonists is increased in schizophrenia, whereas receptors labeled by both antagonists and agonists are increased in animals after prolonged neuroleptic treatment.

Adenylate Cyclase Activity. Some postsynaptic DA receptors (D1-type) are thought to be associated with a DA-sensitive adenylate cyclase (Kebabian, Petzold, and Greengard 1972). Carenzi et al. (1975) reported no significant differences between nine nonpsychiatric controls and seven chronic schizophrenics in the basal or DA-stimulated activity of adenylate cyclase (AC) in post-mortem caudate. This finding concurs with a recent report that the D1 component of ^{3}H-neuroleptic binding was not elevated in post-mortem caudate samples from schizophrenics (Cross, Crow, and Owen 1981). Pandey et al. (1977) found that platelet prostaglandin (PG) E_1-stimulated AC activity was significantly higher in five acute schizophrenics, but not four chronic patients, compared to 10 normals. On the other hand, Rotrosen et al. (1978, 1980) reported significantly lower PGE_1-stimulated activity of platelet AC in both acute ($n = 7$) and chronic ($n = 32$) schizophrenics compared to 29 normals. Kafka and van Kammen (1978) also found a reduced PGE_1-stimulated AC activity in the platelets of male schizophrenics compared to healthy males. Subsequent studies by Pandey's group apparently have not confirmed their initial finding of elevated platelet AC activity in acute schizophrenics (Rotrosen et al. 1978). It is not known if there is any relationship between the activities of brain and platelet AC.

Neuroendocrinology. The generality of the DA hypothesis of schizophrenia has been intensively studied with neuroendocrinologic methods. These studies examine dopaminergic activity in the hypothalamic-pituitary system in order to test for a generalized dopaminergic hyperactivity in the brains of schizophrenics. DA of hypothalamic origin appears to be physiologically involved in the stimulatory control of growth hormone (GH) secretion (Martin 1973) and the tonic inhibitory control of prolactin release (Meites and Clemens 1972; Gudelsky 1981). Two approaches have been used in studies of the hypothalamic-pituitary DA system: (1) basal plasma hormone levels in schizophrenics and controls may reflect a presynaptic hyperactivity or a postsynaptic supersensitivity; (2) the effects of DA agonists on hormone levels might expose a postsynaptic DA receptor supersensitivity in schizophrenics. It should be cautioned that a demonstration of excessive hypothalamic-pituitary DA activity cannot necessarily be used as evidence for hyperactivity of the mesolimbic, mesocortical, and nigrostriatal DA systems (Meltzer et al. 1978).

In general, basal plasma prolactin levels have not differed in acute and chronic schizophrenics compared to controls or to a normal laboratory range (Meltzer, Sachar, and Frantz 1974*a*, 1974*b*; Brambilla et al. 1976; Ettigi et al. 1976; Meltzer and Fang 1976; Johnstone, Crow, and Mashiter 1977; Wode-Helgodt et al. 1977; Cotes et al. 1978; Gruen et al. 1978; Rotrosen et al. 1979; Naber, Ackenheil, and Laakmann 1980). Brambilla et al. (1979*a*) reported "markedly low" basal prolactin levels in 6 of 10 chronic schizophrenics ($p = 0.1$). Most investigators also found that basal GH levels are within the normal range in schizophrenics (Schimmelbusch, Mueller, and Sheps 1971; Vigneri et al. 1974; Cotes et al. 1978; Brambilla et al. 1979*a*; Rotrosen et al. 1979; Meltzer et al. 1980*b*). In contrast, two studies have reported significantly elevated baseline GH in schizophrenics compared to controls (Ettigi et al. 1976; Janowsky et al. 1978). Ettigi et al. (1976) examined 17 chronic schizophrenics who had not received neuroleptics for at least 2 weeks, and Janowsky et al. (1978) studied a mixed group of 19 acute and chronic schizophrenics, most of whom were on neuroleptics. Thus, only 3 of 15 studies are consistent with a generalized DA hypothesis which would predict depressed basal prolactin and elevated basal GH levels in schizophrenics.

Rotrosen et al. (1979) recently reviewed several investigations of the effects of DA agonists on neuroendocrine function in schizophrenics. In their own experience, the plasma GH rise in response to apomorphine was reliable when measured on two or three occasions in the same subjects, whereas the prolactin depression was less reliable (Rotrosen et al. 1979). The authors concluded that prolactin suppression by DA agonists is a poor tool for quantitatively comparing individuals or groups. Studies of the endocrine responses to the indirect DA agonists, *l*-DOPA and amphetamine, produced highly variable results with no clear-cut differences between schizophrenics and controls (Rotrosen, Angrist, and Paquin 1978; Rotrosen et al. 1979). However, a more consistent pattern has emerged from studies of GH responses to apomorphine: significantly exaggerated GH responses were found in drug-free acute schizophrenics, and in those chronic schizophrenics with sporadic or little neuroleptic use (Pandey et al. 1977; Rotrosen et al. 1979). Chronic schizophrenics who had received prolonged neuroleptic treatment showed significantly blunted GH responses to apomorphine (Ettigi et al. 1976; Rotrosen et al. 1976; Tamminga et al. 1977). Similarly, Meltzer and coworkers reported a strong trend for schizophrenics ill less than 4 years to have a larger GH response than controls, whereas those ill 4 or more years tended to have a smaller GH response than controls (Meltzer et al. 1980*b*; Meltzer, Busch, and Fang 1981).

The blunted GH responses in chronic schizophrenics did not seem to be due to residual neuroleptics since the patients in the above studies had been withdrawn from medication for periods ranging from 1 to 15 weeks. Instead, two independent studies found that the blunted responses were statistically related to the total years of previous neuroleptic treatment (Ettigi et al. 1976; Rotrosen et al. 1979). Along this line, Rotrosen et al. (1979) cited animal studies showing hypothalamic-pituitary subsensitivity induced by chronic neuroleptics. They concluded that a similar mechanism could result in the blunted GH responses to apomorphine in chronic schizophrenics. It was also suggested that the exaggerated GH responses in unmedicated acute and chronic schizophrenics may represent a DA receptor supersensitivity that is characteristic of the schizophrenic disease process. This hypothalamic-pituitary receptor supersensitivity may not be reflected in basal hormone levels due to other overriding neuroendocrine control mechanisms. Again, it is not clear if these results represent an isolated DA receptor supersensitivity in the hypothalamic-pituitary system, or if a generalized dopaminergic supersensitivity might exist.

Clinical Effects of Drugs That Alter Dopaminergic Activity

DA Agonists. Various drugs that increase or decrease dopaminergic activity have been given to schizophrenics in clinical tests of the DA hypothesis. Of these agents, DA agonists understandably have been the most intensively studied. The most forthright interpretation of the DA hypothesis would predict an exacerbation of schizophrenic symptomatology by DA agonists. The 24 studies outlined in table 2 appear to have yielded rather complex results, but some patterns in the data can be discerned.

Studies 1–7 (table 2) reported therapeutic improvements when *l*-DOPA or amphetamine was given to chronic schizophrenics in addition to, or instead of, the patients' usual maintenance neuroleptics. Descriptive information revealed that most of these patients had marked "negative" symptoms of withdrawal, motor retardation, and blunted affect. It has been suggested that these results are inconsistent with the DA hypothesis (Alpert and Friedhoff 1980), but the therapeutic improvement in each study largely consisted of a decrease in negative symptoms with little change in psychotic symptomatology. For example, Inanaga et al. (1975) reported that *l*-DOPA increased motivation, active contact, and activity while having little effect on hallucinations and delusions. Cesarec, Eberhard, and Nordgren (1974) found an improved initiative and interest in the surroundings when 15- to 20-mg daily oral doses of amphetamine were added to the neuroleptic regimen. Segal and Janowsky (1978) observed that those patients who improved following a methylphenidate infusion were often chronically deteriorated, chronically hospitalized schizophrenics. In contrast, a recent report indicated that *d*-amphetamine, 0.5 mg/kg orally, did not significantly improve the motor retardation and blunted affect in a group of acute and chronic schizophrenics (Angrist, Rotrosen, and Gershon 1980*a*). The latter patient group appeared to be more actively psychotic than the emotionally withdrawn patients predominating in studies 1–6 (table 2). Thus, the beneficial effect of DA agonists is most commonly seen in the chronically deteriorated patient whose clinical picture is dominated by negative symptoms.

There are at least two ways in which the improvement in negative symptoms can be explained in accord with the DA hypothesis: (1) Meltzer and Stahl (1976) suggested that low doses of DA agonists may counteract the neuroleptic-induced inhibition of dopaminergic activity in DA tracts (e.g., the nigrostriatal) that are not related to the pathogenesis of the psychosis; (2) Kety (1979) proposed that the negative symptoms of schizophrenia may result from a diminished noradrenergic activity. Although *l*-DOPA administration would elevate noradrenergic and dopaminergic activity, the DA effects would be blocked by the neuroleptics.

A clinical worsening was observed in studies 7–19 (table 2) when various DA agonists were given to schizophrenics orally or intravenously (i.v.). These studies included patients with prominent "positive" symptoms (i.e., hallucinations and delusions), unlike most of the patients in studies 1–6. Three groups explicitly described a DA agonist-induced worsening of preexisting positive symptoms (Yaryura-Tobias, Diamond, and Merlis 1970; Janowsky et al. 1973; Angrist and Gershon 1977). These

Table 2. Clinical effects of DA agonists in schizophrenia

Study	Patients (*n*) and diagnostic criteria	DA agonist and neuroleptic treatment	Research design	DA agonist effects
1. Cesarec, Eberhard, and Nordgren (1974)	9 chronic schizophrenics, clinical diagnoses	Amphetamine × 14 days, 15–20 mg/day, p.o., + NL	Open, uncontrolled	Clinical impression of negative symptoms: overall I ($p < .05$), 5 I, 4 NC
2. Buchanan et al. (1975)	14 chronic schizophrenics, clinical diagnoses	*l*–DOPA × 6 weeks, maximum dose = 1,250 mg/day, + NL	Double blind, placebo control	RPRS: overall NS; clinical impression: 8 I, 5 NC, 1 W
3. Gerlach and Luhdorf (1975)	13 simple schizophrenics, clinical diagnoses	*l*–DOPA × 12 weeks, maximum dose = 300–900 mg/day + benserazid 75–225 mg/day, p.o., + NL	Double blind, placebo control, crossover	Total BPRS: Overall I ($p < .05$), 9 I, 3 NC, 1 W; VAWS: overall ↑ activity ($p < .05$)
4. Inanaga et al. (1975)	52 chronic schizophrenics: 38 hebephrenic, 8 paranoid, 2 catatonic, 4 "others," clinical diagnoses	*l*–DOPA × 8 weeks, maximum dose = 300–600 mg/day, p.o., +NL	Double blind, placebo control	"Therapeutic response": overall I ($p < .05$), 26 I, 24 NC, 2 W
5. Ogura, Kishimoto, and Nakao (1976)	94 chronic schizophrenics, clinical diagnoses	*l*–DOPA × 4.6 months (average), maximum dose = 150–1,600 mg/day, + NL	Open, uncontrolled	"Therapeutic effect": 21 I, 69 NC, 4 W
6. Brambilla et al. (1979b)	6 chronic hebephrenic schizophrenics, WHO	*l*–DOPA × 30 days, maximum dose = 2 g/day + carbodopa, 200 mg/day, p.o., – NL	Double blind, placebo control	Modified WRS scores of affective disorder, active behavior, and maladjustment to reality: overall NS, 2 I, 4 NC
7. Calil, Yesavage, and Hollister (1977)	3 chronic schizophrenics: 2 undifferentiated, 1 paranoid, RDC	*l*–DOPA × 1–6 weeks, maximum dose = 500 mg/day, p.o., + NL	Open, uncontrolled	BPRS: 2 ↑ psychosis, 1 ↓ negative symptoms
8. Alpert et al. (1978)	8 chronic schizophrenics: 5 undifferentiated, 3 paranoid, *DSM–II*	*l*–DOPA × 24 days, maximum dose = 6 g/day, –NL	Open, chlorpromazine control	BPRS scores: overall NS; "clinical condition": generally worse and resembling a "diffuse toxic psychosis"
9. Yaryura-Tobias, Diamond, and Merlis (1970)	5 chronic schizophrenics: 3 undifferentiated, 2 paranoid, clinical diagnoses	*l*–DOPA × 3 weeks, maximum dose = 2 g/day, p.o., + NL	Open, placebo control	Clinical impression: 4 ↑ hallucinations, 1 ↑ activity
10. Angrist, Sathananthan, and Gershon (1973); Angrist et al. (1977)	10 schizophrenics: 3 acute, 5 chronic, 2 schizoaffective, clinical diagnoses	*l*-DOPA × 3 weeks, maximum dose = 3–6 g/day, – NL	Open, placebo control	BPRS, clinical impression: 7 ↑ psychosis, 3 "nonspecific stimulation"

Table 2. Clinical effects of DA agonists in schizophrenia—*Continued*

Study	Patients (*n*) and diagnostic criteria	DA agonist and neuroleptic treatment	Research design	DA agonist effects
11. Janowsky et al. (1973)	22 "actively ill" schizophrenics: 5 chronic undifferentiated, 4 acute, 5 schizoaffective, 7 paranoid, 1 catatonic, *DSM–II*	Methylphenidate, 0.5 mg/kg, i.v., + NL and − NL	Double blind, placebo control	Modified B-H; overall ↑ psychosis ($p <$ .00003) at + 15 minutes, results unaffected by NL
12. Angrist et al. (1975, 1977)	7 schizophrenics: 1 acute paranoid, 4 chronic undifferentiated, 2 schizoaffective, clinical diagnoses	ET–495 × 6–18 days, maximum dose = 80–320 mg/day, p.o., − NL	Open, uncontrolled	BPRS scores: overall NS; clinical impression: 4 ↑ psychosis, 2 NC, 1 ↓ psychosis
13. Davis and Janowsky (1973); Janowsky and Davis (1974, 1976)	16 "actively ill" schizophrenics, *DSM–II*	Single i.v. injections of 29 mg methylphenidate, 10–20 mg *d*-amphetamine, 28 mg *l*-amphetamine (no information on NL)	Double blind, placebo control, crossover	5-pt. scale: overall ↑ psychosis and activation scores ($p <$ .05) at + 10–20 minutes after all drugs
14. Janowsky et al. (1977); Janowsky, Huey, and Storms (1977)	16 "actively psychotic" schizophrenics, *DSM–II*	Methylphenidate, 0.5 mg/kg, i.v., + NL	Double blind, nonpsychotic inpatient control group	Schizophrenics: overall ↑ global psychosis ratings and pathologic responses in word association and ink blot tests ($p <$ .05) at + 15 minutes
15. Small et al. (1977)	5 chronic schizophrenics, RDC	Lergotrile × 3–14 days, maximum dose = 6–8 mg/day, + NL	Double blind, antiparkinsonism drug control	BPRS and clinical impression: 5 ↑ psychosis
16. Trabucchi et al. (1977)	12 patients with "various psychotic syndromes, mostly schizophrenia," clinical diagnoses	Bromocriptine × 1 week, 15 or 37.5 mg/day, − NL	Open, uncontrolled	BPRS: overall NS. Tendency toward ↑ psychotic symptoms after the high dose
17. Tamminga and Schaffer (1979)	12 chronic schizophrenics including schizoaffective, undifferentiated, paranoid, RDC	Bromocriptine (10 mg/day) or CF 25–397 (60 mg/day) × 3 weeks, p.o., + NL and − NL	Double blind, placebo control, crossover	Modified NHSI: ↑ psychosis in 3 of 7 patients after bromocriptine, NC after CF 25–397, results were unaffected by NL
18. Angrist, Rotrosen, and Gershon (1980*a*, 1980*b*)	21 schizophrenics: 2 acute, 8 subacute, 4 subchronic, 7 chronic, RDC	*d*-Amphetamine, 0.5 mg/kg, p.o., − NL	Open, uncontrolled	Overall ↑ in total BPRS ($p <$ .01) and positive symptoms ($p <$ .001); total BPRS: 17 W, 3 I, 1 NC
19. van Kammen and Bunney (1979)	19 schizophrenics, 27 schizoaffective, RDC	*d*-Amphetamine, 20 mg, i.v., − NL	Double blind, placebo control	Modified B-H psychosis scores: overall NS, 18 W, 14 I, 14 NC

Table 2. Clinical effects of DA agonists in schizophrenia—*Continued*

Study	Patients (n) and diagnostic criteria	DA agonist and neuroleptic treatment	Research design	DA agonist effects
20. Corsini et al. (1977)	58 schizophrenics: 24 paranoid, 4 catatonic, 18 schizoaffective, 12 hebephrenic, clinical diagnoses	Apomorphine, 1 mg, i.m., − NL	Open, uncontrolled	Modified BPRS: 21 ↓ psychosis lasting 20-50 minutes
21. Smith, Tamminga, and Davis (1977)	4 chronic schizophrenics, RDC	Apomorphine, 1.5–6 mg, s.c. or p.o., + NL and − NL	Double blind, placebo control	NHSI: 3 ↓ psychosis and 1 slight worsening at + 20 and + 40 minutes, results were unaffected by NL
22. Tamminga et al. (1978)	18 chronic schizophrenics: 7 undifferentiated, 6 paranoid, 5 schizoaffective, RDC	Apomorphine, 3 mg, s.c., + NL	Double blind, placebo control	Modified NHSI: overall ↓ psychosis ($p <$ .02) at + 30 to + 60 minutes, 9 I, 4 NC, 5 slight W
23. Hollister, Davis, and Berger (1980)	11 schizophrenics, RDC	Apomorphine × 2 weeks, 20 mg/day, p.o., +NL	Blind, placebo control	BPRS: generally NC in psychosis
24. Kornetsky (1976)	25 chronic schizophrenics, clinical diagnoses	*d*-Amphetamine × 4–7 days, maximum dose = 20–40 mg/day, p.o., − NL	Double blind, placebo control	Clinical impression: NC in psychosis

Abbreviations: WHO = World Health Organization (1977); *DMS-II* = *Diagnostic and Statistical Manual of Mental Disorders-II* (American Psychiatric Association 1968); RDC = Research Diagnostic Criteria (Spitzer, Endicott, and Robins 1975); WRS = Wittenborn Rating Scale (Brambilla et al. 1979b); BPRS = Brief Psychiatric Rating Scale (Overall and Gorham 1962); RPRS = Rating Scale of Rockland and Pollin (1965); VAWS = Activity—Withdrawal Scale of Venables (1957); B-H = Bunney-Hamburg Scale of Psychiatric Symptoms (Bunney and Hamburg 1963); NHSI = New Haven Schizophrenia Index (Astrachan et al. 1972); +/− NL = patients were on or off neuroleptics during the study; p.o. = orally; i.v. = intravenously; i.m. = intramuscularly; s.c. = subcutaneously; I = improved; NC = no change; W = worsened; NS = nonsignificant.

An effort was made to identify unique subject groups.

results did not seem to be affected by the presence or absence of concurrent neuroleptic medication (Janowsky et al. 1973). Two reports did not support a specific ability of *l*-DOPA to exacerbate schizophrenic symptoms (Gjessing 1975; Alpert et al. 1978). Alpert et al. (1978) felt that the worsening in their patients' condition resembled a "diffuse toxic psychosis" rather than an aggravation of schizophrenic psychosis. At a recent conference, Gjessing (1975) stated:

> . . . I have not seen any worsening of the [schizophrenic] symptoms with . . . as much as 13 grams of dopa. [p. 84]

This report was not accompanied by any description of the patient population or the duration of treatment.

Angrist's group also administered DA agonists to normals and nonschizophrenic psychiatric inpatients (Sathananthan, Angrist, and Gershon 1973; Angrist et al. 1977; Angrist and Gershon 1977). They found that schizophrenics were much more sensitive to the psychotogenic effects of *l*-DOPA and *d*-amphetamine, leading to the conclusion that schizophrenics and nonschizophrenics may represent a continuum of varying thresholds to dopaminergic stimulation that can be tolerated without psychosis (Sathananthan, Angrist, and Gershon 1973). Such a continuum does not seem to apply to the apomorphine emesis threshold, however, since the latter parameter did not significantly differ between 21 schizophrenics and 10 nonschizophrenic controls (Angrist, Kotrosen, and Gershon 1980*b*).

The failure to find a universal biochemical defect among schizophrenics has contributed toward the consideration of multiple disease entities as a basis for the "schizophrenias" (Buchsbaum and Haier 1978; Hornykiewicz 1978; Meltzer 1979; Crow 1980; Berger 1981). With heterogeneity as a possibility, some researchers have begun attempts at identifying biologically homogeneous subgroups within the schizophrenic population (Wyatt et al. 1981; Jeste et al. 1982). Thus, among schizophrenic subjects, a positive family history of schizophrenia was significantly related to low plasma DBH activity (Baron, Levitt, and Perlman 1980) and high CSF HVA (Sedvall and Wode-Helgodt 1980). Elevated CSF HVA was also associated with poor premorbid sexual adjustment in a group of schizophrenics (Leckman, Bowers, and Sturges 1981). Low CSF HVA was correlated with poor prognosis (Bowers 1974) and the presence of first-rank symptoms (Bowers 1973; Post et al. 1975). The presence of auditory hallucinations and paranoid features may discriminate chronic schizophrenics with decreased platelet MAO activity (Wyatt et al. 1980; Jeste et al. 1982).

Based on clinical phenomenology, Crow (1980) has distinguished two syndromes among patients with diagnoses of schizophrenia:

> The first (the type I syndrome, equivalent to "acute schizophrenia," and characterised by the positive symptoms—delusions, hallucinations, and thought disorder) is in some way associated with a change in dopaminergic transmission; the second process (the type II syndrome, equivalent to the "defect state," and characterised by the negative symptoms—affective flattening and poverty of speech) is unrelated to dopaminergic transmission but may be associated with intellectual impairment and, perhaps, structural changes in the brain . . . [Type I symptoms] predict a potential response to neuroleptics; [type II symptoms] are more closely associated with a poor long-term outcome. Episodes of type I symptoms may be followed by development of the type II syndrome, and both may be present together. Type II symptoms . . . occasionally occur in the absence of the type I syndrome. . . . [p. 68]

Crow's type I symptoms are similar to the first-rank symptomatology of Schneider, while the type II symptoms correspond to the fundamental schizophrenic symptoms of Kraepelin and Bleuler (Mackay and Crow 1980).

Crow's hypothetical subgroups are tentatively supported by pharmacological, neuroendocrinological, and neuroradiological evidence. On the basis of drug responses, the type I and type II syndromes resemble, respectively, the neuroleptic/AMPT-responsive and -resistant subgroups of Nasrallah et al. (1977, 1980). Nasrallah's subgroups were felt to be indistinguishable on standard diagnostic criteria, but it was noted that six of seven neuroleptic/AMPT-resistant patients had evidence of lateral cerebral ventricular enlargement on computerized tomographic scans (Nasrallah et al. 1980). Schizophrenics with normally sized cerebral ventricles are most apt to exhibit a correlation between psychosis scores and central dopaminergic activity as reflected in plasma prolactin levels (Kleinman et al. 1982). The increased ventricular size in patients with (1) negative symptoms (Johnstone et al. 1978*b*; Andreasen et al. 1982), (2) neuroleptic/AMPT resistance (Nasrallah et al. 1980), and (3) lack of a correlation between psychosis and dopaminergic activity (Kleinman et al. 1982) supports the existence of a subgroup (Crow type II) whose illness is related to structural changes in the brain rather than an altered dopaminergic transmission. A neuroleptic/AMPT-responsive subgroup (Crow type I) seems more likely to be associated with a dopaminergic dysfunction (Carlsson et al. 1972*b*, 1973; Magelund, Gerlach, and Casey 1979).

A nondopaminergic etiology might also explain the absence of psychosis-exacerbation after DA agonist (Kornetsky 1976; Segal and Janowsky 1978) and MAOI (Brenner and Shopsin 1980) administration to chronically hospitalized schizophrenics. In fact, the predominant response to DA agonists in a significant proportion of chronic schizophrenics appears to be an improvement in negative symptoms (Cesarec, Eberhard, and Nordgren 1974; Buchanan et al. 1975; Gerlach and Luhdorf 1975; Inanaga et al. 1975; Ogura, Kishimoto, and Nakao 1976). Foreshadowing Crow's formulation, Segal and Janowsky (1978) suggested that the dichotomous (improvement vs. worsening) responses to DA agonists may reflect at least two different types of schizophrenia. Brambilla et al. (1979*b*) also felt that the dichotomous responses indicated "two different disease processes."

Van Kammen and Bunney (1979) observed a differential response to *d*-amphetamine that appeared to be related to the initial clinical condition of the schizophrenics. A single i.v. injection produced a worsening in patients with relatively low initial psychosis scores, while severely psychotic patients actually improved (van Kammen et al. 1977). The authors suggested that the improvement in psychosis may be due to a feedback regulatory process affected by *d*-amphetamine.

Another explanation for the antipsychotic effect of *d*-amphetamine (van Kammen and Bunney 1979) could be a reduction in the sensitivity of postsynaptic DA receptors. We have shown that a single dose of *d*-amphetamine can reverse the neuroleptic-induced behavioral supersensitivity to apomorphine in rats (Haracz and Tseng 1980). Other animal studies also found that chronic *l*-DOPA treatment reduces the dopaminergic supersensitivity induced by neuroleptics (Friedhoff, Bonnet, and Rosengarten 1977; Ezrin-Waters and Seeman 1978; List and Seeman 1979). Alpert et al. (1978) gave *l*-DOPA therapy for several weeks to a group of schizophrenics with tardive dyskinesia. They reported an initial worsening of both "mental condition" and dyskinetic symptoms, followed by a habituation and reduction in dyskinetic symptoms, with the maximum response occurring after discontinuation of *l*-DOPA. The "chronic schizophrenic process" appeared to follow the same course as the dyskinesia in several patients. If this result represents a reduction in psychotic symptoms after *l*-DOPA, then it could provide evidence that a postsynaptic supersensitivity is an etiological agent in schizophrenia. However, Alpert et al. (1978) observed only a slight, nonsignificant improvement in the psychosis ratings of eight chronic schizophrenics at termination, and 4 days after termination, of chronic *l*-DOPA treatment. Furthermore, three other studies found only a return to baseline, without an improvement in schizophrenic psychosis, at 1 to 10 days after termination of DA agonist treatment (Yaryura-Tobias, Diamond, and Merlis 1970; Janowsky, Huey, and Storms 1977; Small et al. 1977). Thus, the effect of DA agonists on the sensitivity of postsynaptic DA receptors in schizophrenia requires further clarification.

Studies 19–22 (table 2) indicate that DA agonists can yield an improvement in schizophrenic psychosis under certain conditions. Neuroleptics did not appear to alter the antipsychotic effect of apomorphine (Smith, Tamminga, and Davis 1977; Tamminga et al. 1978). A potent apomorphine analog, *N-n*-propylnorapomorphine, also ameliorates psychotic symptoms (Tamminga et al. 1981).

The improvement after low-dose apomorphine has been explained (in line with the DA hypothesis) as resulting from a preferential stimulation of presynaptic DA receptors (Cutler et al. 1981). One group studied the clinical effect of two ergot derivatives, bromocriptine and CF 25–397, which are less active than apomorphine at the presynaptic DA receptor (Tamminga and Schaffer 1979; Tamminga et al. 1979). Low doses of these DA agonists had no antipsychotic effect; in fact three of seven schizophrenics worsened while receiving bromocriptine. Trabucchi et al. (1977) also found that bromocriptine tended to worsen psychotic symptoms. On the other hand, no antipsychotic effect was seen when apomorphine was given orally over a 2-week period (Hollister, Davis, and Berger 1980). The latter group found that high oral doses of apomorphine (up to 120 mg/day) actually aggravated the psychotic symptoms of two schizophrenics. Apparently, high-dose apomorphine has significant postsynaptic activity. Differences in doses and routes of administration may account for the variety of responses to apomorphine in studies 20–23 (table 2).

Finally, Kornetsky (1976; table 2) found that multiple oral doses of *d*-amphetamine did not affect the psychotic symptomatology of 25 chronically hospitalized schizophrenics. Cesarec, Eberhard, and Nordgren (1974) similarly failed to find any worsening psychosis in nine chronic schizophrenics during a 14-day regimen of oral amphetamine. It seems that a particular population of chronic schizophrenics, possibly prevalent in chronic-care institutions, may be unresponsive to the psychotogenic effect of DA agonists.

MAO Inhibitors. Brenner and Shopsin (1980) pointed out that current biochemical constructs of schizophrenia would predict an aggravation of schizophrenic symptoms by the administration of an MAO inhibitor (MAOI). They recently reviewed 14 investigations in which 281 chronic schizophrenics were exclusively treated with MAOIs. Global treatment outcome was reported as unchanged in 71 percent of the patients, improved in 26 percent, and worsened in only 3 percent. A statistically significant tendency was found for patients to be rated as "improved" only when hallucinations and delusions were not evaluated in a given study. Thus, a reduction in negative symptoms accounted for most of the improvement, although some patients were described as showing improvement in hallucinations and delusions under open study conditions.

It is surprising, in terms of the DA hypothesis, that MAOIs failed to exacerbate psychotic symptoms in the vast majority of patients. The reviewers emphasized that, in comparison with the usual antidepressant MAOI regimens, the schizophrenic populations were generally treated with higher dosages of MAOIs for longer trial periods (Brenner and Shopsin 1980). However, none of the investigations included assays of MAO activity in the patients under treatment. Therefore, it is impossible to determine if the negative results were secondary to an incomplete MAO inhibition. Youdim (1979) reported that 85 percent of rat brain MAO activity must be inhibited before a hyperactivity syndrome occurs in response to *l*-DOPA or *l*-tryptophan treatment. Mendlewicz and Youdim (1978) measured the platelet MAO activities of 14 depressed patients who were undergoing a 40-day antidepressant regimen of 5-hydroxytryptophan plus deprenyl, an MAOI. A platelet MAO inhibition of less than 85 percent was found only in the four nonresponding patients, indicating that the level of MAO inhibition is a critical determinant of the observed psychological effects. The schizophrenia studies employed MAOIs other than deprenyl, so it would be difficult to use the depressed patients' deprenyl dosage as a yardstick of adequate MAO inhibition. An 85 percent criterion of significant MAO inhibition also makes one wonder about the functional significance of the platelet MAO deficits in chronic schizophrenics, which were usually reported as less than 50 percent (Wyatt et al. 1980).

Aside from the question of adequate MAO inhibition, the DA hypothesis appears to be challenged by the improvement of psychosis in some schizophrenics. In defense of the DA hypothesis, it can be speculated that chronic MAOI treatment may reduce DA receptor sensitivity, as demonstrated in rats after chronic *l*-DOPA (Friedhoff, Bonnet, and Rosengarten 1977; Ezrin-Waters and Seeman 1978; List and Seeman 1979), thereby reducing psychotic symptoms. Alternatively, the clinical improvement after MAOIs and DA agonists (studies 1–7, table 2) may indicate that central dopaminergic transmission is either decreased or is not a primary etiologic factor in some chronic schizophrenics. A large proportion of the schizophrenics in the MAOI investigations were chronically hospitalized, as were the patients studied by Kornetsky (1976). Hence, more support is lent to the hypothesis that chronically deteriorated schizophrenics are hyporesponsive to the psychotogenic effects of elevated dopaminergic transmission.

α-Methyl-*p*-Tyrosine (AMPT) and α-Methyldopa (AMD). AMPT decreases catecholamine synthesis by inhibiting TOH, the rate-limiting enzyme of the synthetic pathway (Goodman and Gilman 1975). The catecholamine-depleting mechanism of AMD is not so well established, although the inhibition of TOH may also be involved (Meltzer and Stahl 1976). The reduction of brain DA concentrations produced by these drugs should result in a favorable clinical outcome in schizophrenics according to the DA hypothesis.

Two early studies showed an overall lack of antipsychotic effect when AMPT was the only drug administered to acute and chronic schizophrenics (Gershon et al. 1967; Charalampous and Brown 1967). Each study found decreases in urinary catecholamine metabolites that indicated some inhibition of TOH activity, but it is not known if central dopaminergic activity was significantly inhibited.

Carlsson's group reported that AMPT treatment allowed a 60- to 79-percent mean reduction in the neuroleptic dose required to control psychotic symptoms in eight chronic schizophrenics (Carlsson et al. 1972*b*, 1973; Walinder et al. 1976). This finding was replicated by Magelund, Gerlach, and Casey (1979), but not by Nasrallah et al. (1977) and Gillin et al. (1979). Magelund, Gerlach, and Casey (1979) studied 12 chronic schizophrenics whose psychotic symptoms had been exacerbated by a 67-percent mean reduction in their neuroleptic dosage. Compared to a placebo, AMPT significantly decreased the subjects' total Brief Psychiatric Rating Scale (BPRS) scores.

Nasrallah and colleagues obtained negative results when they studied 14 chronic schizophrenics (Nasrallah et al. 1977; Gillin et al. 1979). Each of these patients had a prolonged illness which was only moderately responsive to neuroleptic therapy. The addition of AMPT treatment did not affect the patients' BPRS psychosis scores, even though an inhibition of DA synthesis was suggested by the elevations in plasma prolactin levels. Nasrallah et al. (1980) proposed that the conflict with previous studies could be explained by the postulation of two subgroups of chronic schizophrenics: a neuroleptic/AMPT-resistant group, represented by their own patients who had shown little response to full maintenance dosages of neuroleptics; and a neuroleptic/AMPT-responsive group, such as the patients of Carlsson et al. (1972*b*, 1973). In agreement with this hypothesis, the AMPT-responding patients of Magelund, Gerlach, and Casey (1979) apparently were also responsive to their initial maintenance neuroleptic dosages.

AMD, like AMPT, did not have a significant antipsychotic effect when administered alone to chronic schizophrenics (Herkert and Keup 1969; Pecknold et al. 1972). Neither of these studies included an assessment of the effect of AMD on the catecholamine metabolism in the patients. Chouinard et al. (1973) reported that AMD plus chlorpromazine significantly improved the psychopathology in 8 of 10 chronic schizophrenics who were unresponsive to their previous antipsychotic medication. Thus, it appears that both AMPT and AMD can potentiate the antipsychotic action of neuroleptics in at least a subgroup of chronic schizophrenics. These results offer additional indirect pharmacological support for the DA hypothesis.

Summary and Conclusion

The abundant generation of data indicates that the DA hypothesis of schizophrenia has been an extremely successful heuristic device. However, this research activity has not produced a solid body of confirmatory evidence for the hypothesis. Indirect pharmacological evidence still makes up the bulk of the support, despite the extensive study of tissue samples obtained from schizophrenics. Direct support is either uncompelling or has not been widely replicated. In post-mortem studies, for example, there are at least as many negative findings as there are positive reports of elevated brain DA levels in schizophrenics (table 1).

The most widely replicated biochemical finding in schizophrenia has been the low peripheral MAO activity in chronic schizophrenics (Buchsbaum, Coursey, and Murphy 1980). The elevated PEA found in the urine of chronic paranoid schizophrenics may reflect the functional significance of an MAO deficiency. Still, one might question the etiological significance of a deficient enzyme activity that is generally only 30-50 percent less than normal (Wyatt et al. 1980), is frequently found in normal subjects (Buchsbaum, Coursey, and Murphy 1976; Murphy et al. 1977), and is possibly associated with neuroleptic treatment (Chojnacki et al. 1981; DeLisi et al. 1981*b*; Sahai, Arora, and Meltzer 1981). Moreover, no behavioral improvements were produced by dietary and pharmacological methods that successfully decreased PEA in schizophrenics (Wyatt, Bigelow, and Gillin 1979).

The hypothesis that schizophrenics have supersensitive brain DA receptors receives some direct support and is also consistent with some indirect pharmacological evidence. Four out of five laboratories have reported elevated ^{3}H-neuroleptic binding in the post-mortem brain samples of schizophrenics (Lee et al. 1978; Owen et al. 1978; Mackay et al. 1980*a*; Reisine et al. 1980*b*; Reynolds et al. 1981). Three of these laboratories (Owen et al. 1978; Lee and Seeman 1980*b*; Reisine et al. 1980*b*), but not the other two (Mackay et al. 1980*b*; Reynolds et al. 1981), also found increased ^{3}H-neuroleptic binding in specimens from a small number of drug-free patients. Exaggerated GH responses to apomorphine were observed in acute and chronic schizophrenics who had received little or no neuroleptic therapy (Rotrosen et al. 1979). Schizophrenics seem to be more sensitive than normals to the psychotogenic effect (Angrist and Gershon 1977), but not the emetic effect (Angrist, Rotrosen, and Gershon 1980*b*), of DA agonists.

If the psychotogenic effect of DA agonists is related to the sensitivity of DA receptors, then neuroleptic withdrawal should heighten the sensitivity of schizophrenics to DA agonists (van Kammen et al. 1980). Evidence of DA receptor supersensitivity has been found in animals shortly after the cessation of chronic neuroleptic treatment (Muller and Seeman 1978; Haracz and Tseng 1980). However, a group of schizophrenics did not develop a supersensitivity to the psychosis-worsening effect of *d*-amphetamine after pimozide withdrawal (van Kammen and Bunney 1979; van Kammen et al. 1980). Thus, the hypothesized DA receptor supersensitivity in schizophrenia is challenged by some negative findings (Angrist, Rotrosen, and Gershon 1980*b*; van Kammen et al. 1980; Reynolds et al. 1981) and by the possibility that the elevated ^{3}H-neuroleptic binding is drug-related (Mackay et al. 1980*b*; Snyder 1981).

The DA hypothesis of schizophrenia will require adjustment if compelling evidence for a gross disturbance in DA function is not forthcoming. Some modifications that stay consistent with the pharmacological foundations include: (1) an isolated dopaminergic abnormality in a discrete brain area; (2) a primary disturbance in another neurotransmitter system that interacts with a dopaminergic system; (3) relatively subtle abnormalities in several aspects of dopaminergic transmission (e.g., MAO deficiency, DA receptor supersensitivity) which synergistically yield a serious abnormality; (4) several "schizophrenias," each with a different dopaminergic dysfunction, so that a sample of the entire group does not show significant changes.

The failure to find a universal biochemical defect among schizophrenics has contributed toward the consideration of multiple disease entities as a basis for the "schizophrenias" (Buchsbaum and Haier 1978; Hornykiewicz 1978; Meltzer 1979; Crow 1980; Berger 1981). With heterogeneity as a possibility, some researchers have begun attempts at identifying biologically homogeneous subgroups within the schizophrenic population (Wyatt et al. 1981; Jeste et al. 1982). Thus, among schizophrenic subjects, a positive family history of schizophrenia was significantly related to low plasma DBH activity (Baron, Levitt, and Perlman 1980) and high CSF HVA (Sedvall and Wode-Helgodt 1980). Elevated CSF HVA was also associated with poor premorbid sexual adjustment in a group of schizophrenics (Leckman, Bowers, and Sturges 1981). Low CSF HVA was correlated with poor prognosis (Bowers 1974) and the presence of first-rank symptoms (Bowers 1973; Post et al. 1975). The presence of auditory hallucinations and paranoid features may discriminate chronic schizophrenics with decreased platelet MAO activity (Wyatt et al. 1980; Jeste et al. 1982). Schizophrenics with a positive family history of schizophrenia did not differ in platelet MAO activity from schizophrenics with no such family history (Belmaker et al. 1978).

Based on clinical phenomenology, Crow (1980) has distinguished two syndromes among patients with diagnoses of schizophrenia:

> The first (the type I syndrome, equivalent to "acute schizophrenia," and characterised by the positive symptoms—delusions, hallucinations, and thought disorder) is in some way associated with a change in dopaminergic transmission; the second process (the type II syndrome, equivalent to the "defect state," and characterised by the negative symptoms—affective flattening and poverty of speech) is unrelated to dopaminergic transmission but may be associated with intellectual impairment and, perhaps, structural changes in the brain . . . [Type I symptoms] predict a potential response to neuroleptics; [type II symptoms] are more closely associated with a poor long-term outcome. Episodes of type I symptoms may be followed by development of the type II syndrome, and both may be present together. Type II symptoms . . . occasionally occur in the absence of the type I syndrome. . . . [p. 68]

Crow's type I symptoms are similar to the first-rank symptomatology of Schneider, while the type II symptoms correspond to the fundamental schizophrenic symptoms of Kraepelin and Bleuler (Mackay and Crow 1980).

Crow's hypothetical subgroups are tentatively supported by pharmacological, neuroendocrinological, and neuroradiological evidence. On the basis of drug responses, the type I and type II syndromes resemble, respectively, the neuroleptic/AMPT-responsive and -resistant subgroups of Nasrallah et al. (1977, 1980). Nasrallah's subgroups were felt to be indistinguishable on standard diagnostic criteria, but it was noted that six of seven neuroleptic/AMPT-resistant patients had evidence of lateral cerebral ventricular enlargement on computerized tomographic scans (Nasrallah et al. 1980). Schizophrenics with normally sized cerebral ventricles are most apt to exhibit a correlation between psychosis scores and central dopaminergic activity as reflected in plasma prolactin levels (Kleinman et al. 1982). The increased ventricular size in patients with (1) negative symptoms (Johnstone et al. 1978*b*; Andreasen et al. 1982), (2) neuroleptic/AMPT resistance (Nasrallah et al. 1980), and (3) lack of a correlation between psychosis and dopaminergic activity (Kleinman et al. 1982) supports the existence of a subgroup (Crow type II) whose illness is related to structural changes in the brain rather than an altered dopaminergic transmission. A neuroleptic/AMPT-responsive subgroup (Crow type I) seems more likely to be associated with a dopaminergic dysfunction (Carlsson et al. 1972*b*, 1973; Magelund, Gerlach, and Casey 1979).

A nondopaminergic etiology might also explain the absence of psychosis-exacerbation after DA agonist (Kornetsky 1976; Segal and Janowsky 1978) and MAOI (Brenner and Shopsin 1980) administration to chronically hospitalized schizophrenics. In fact, the predominant response to DA agonists in a significant proportion of chronic schizophrenics appears to be an improvement in negative symptoms (Cesarec, Eberhard, and Nordgren 1974; Buchanan et al. 1975; Gerlach and Luhdorf 1975; Inanaga et al. 1975; Ogura, Kishimoto, and Nakao 1976). Foreshadowing Crow's formulation, Segal and Janowsky (1978) suggested that the dichotomous (improvement vs. worsening) responses to DA agonists may reflect at least two different types of schizophrenia. Brambilla et al. (1979*b*) also felt that the dichotomous responses indicated "two different disease processes."

In retrospect, it appears that two of the pharmacological cornerstones of the DA hypothesis actually apply only to a subgroup of schizophrenics. The presence of type I symptoms may be a necessary condition for a therapeutic response to neuroleptics and a psychosis-worsening response to DA agonists. For example, *d*-amphetamine, *l*-DOPA, and methylphenidate worsened preexisting positive symptoms (Janowsky et al. 1973; Angrist and Gershon 1977), while patients in remission showed little response to methylphenidate (Janowsky et al. 1973). DA agonists rarely induced psychotic symptoms in patients whose clinical picture was dominated by negative symptoms (Cesarec, Eberhard, and Nordgren 1974; Gerlach and Luhdorf 1975; Inanaga et al. 1975; Brambilla et al. 1979*b*). An oft-repeated clinical observation has been the poor response of negative symptoms to neuroleptic therapy (Letemendia and Harris 1967; Johnstone et al. 1978*a*; Angrist, Rotrosen, and Gershon 1980*a*). To summarize, patients with active positive symptoms generally show a psychotogenic response to DA agonists and a therapeutic response to neuroleptics as predicted by the DA hypothesis. In opposition to the hypothesis, patients with mostly negative symptoms exhibit a beneficial activation in response to DA agonists and little or no clinical change after neuroleptic administration.

The divergent drug responses summarized above may hint at separate etiologies for positive and negative symptoms. Consistent with this notion, both cerebral ventricular size and regional cerebral blood flow appear to vary according to the presence of positive and negative symptoms in subchronic to chronic schizophrenia (Ingvar 1980; Andreasen et al. 1982). By applying the ^{133}Xenon clearance technique to 40 chronic schizophrenics, Ingvar (1980) found that the more inactive, mute, and autistic the patients were, the lower was the cerebral blood flow in the frontal regions of their brains. Elevated flow in postcentral regions was significantly related to cognitive disturbance including hallucinatory activity. Since cerebral blood flow correlates with neuronal activity, it seems that positive and negative symptoms are associated with different regional patterns of neurobiological activity. In addition, Andreasen et al. (1982) reported that a subgroup of schizophrenics with large cerebral ventricles (more than one standard deviation above the control mean) had a preponderance of negative symptoms. The schizophrenics with the smallest cerebral ventricles (well within the control range) exhibited mainly positive symptoms.

The data reviewed above suggest that schizophrenics with predominantly positive (type I) or negative (type II) symptoms also tend to differ in their: (1) clinical responses to DA agonists and antagonists, (2) regional cerebral blood flow patterns, and (3) cerebral ventricular size. Thus, Crow's type I/type II distinction could be a useful theoretical framework in the search for biologically homogeneous subgroups. Biological researchers should carefully characterize the positive and negative symptoms exhibited by their schizophrenic subjects since the two symptom types may result from different pathophysiological processes. Longitudinal studies which relate changes in symptoms to changes in the above pharmacological and neuroradiological parameters may be especially revealing.

The DA hypothesis not only appears to be limited in the range of patients to which it applies, but it is also restricted in theoretical scope. The hypothesis does not readily account for social aspects of schizophrenia (Wing 1978) or the biogenesis of specific schizophrenic symptoms. A full explanation of the disorder must deal with genetic data (Gottesman and Shields 1976) as well as environmental effects on the schizophrenic process (Wynne et al. 1977; Dohrenwend and Egri 1981). Kety (1972) and Bowers (1980) have pointed out that the DA hypothesis (or any other biological hypothesis of schizophrenia) must be related through some mechanism to the complex clinical phenomenology. In this regard, some authors have proposed that an attentional disorder in schizophrenia may be linked to a dopaminergic influence on the focus of attention (Matthysse 1977, 1978; Joseph, Frith, and Waddington 1979). No comprehensive biological scheme has yet been proposed to draw together the genetic, environmental, and clinical features of schizophrenia.

As in most medical research, relatively simple factors have initially been tested as possible causes of schizophrenia. A common early viewpoint was that one abnormal biological factor could produce psychopathology. In search of the abnormality, various authors proposed and tested at least 18 different catecholamine-related theories of schizophrenia (reviewed by Wyatt, Bigelow, and Gillin 1979). Research unrelated to catecholamines further multiplied the number of biological entities under examination. Although it is important to test a reasonable variety of potential markers, eventually it may become necessary to contemplate more complex neurophysiological processes. If one considers the significance of environmental influences in schizophrenia (Kety 1978; Singer, Wynne, and Toohey 1978; Wing 1978), a fruitful research concern may be the adaptation of neuronal circuitry to environmental changes. Animal studies indicate that important behavioral effects can be generated by environmentally induced synaptic modifications (Rosenzweig 1971; Cragg 1975; van Hof-van Duin 1976; Cotman 1978; Hubel 1978; Schwartz and Rothblat 1980). Laboratory methods typically employed in schizophrenia research might not be sensitive to alterations in the function of certain key synapses. Attention to neurophysiological adaptations, perhaps in animal models of psychopathology, may lead to a more meaningful experimental design.

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Measurement of Premorbid Adjustment in Chronic Schizophrenia

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Abstract

The Premorbid Adjustment Scale (PAS) is a rating scale which was developed to be applicable in a research setting. It is designed to evaluate the degree of achievement of developmental goals at each of several periods of a subject's life before the onset of schizophrenia. A description of the scale and its use is presented, along with a discussion of psychometric properties. The PAS has been found to be useful in identifying patients likely to become chronically hospitalized or at high risk for readmission. It may also serve as a possible predictor of patients with brain abnormalities on a computerized tomography (CT) scan.

Schizophrenia markedly disrupts an individual's psychosocial functioning. Assessment of psychosocial functioning has become a useful area of investigation but is confounded by the schizophrenic process itself. Therefore, considerable research has focused on assessment of the individual's psychosocial functioning before the onset of the schizophrenic illness, i.e., the premorbid period. Separating early morbid functioning from premorbid functioning can be difficult at times. To the degree that this separation can be made, one can relate factors preceding the disorder to aspects of the disorder itself, such as course, degree of response to treatment, and current symptoms. Do patients with good premorbid psychosocial functioning have better outcomes or require less medication? Are different etiologies suggested by different patterns of premorbid adjustment? Thoughtful planning of therapeutic goals for psychotic patients requires understanding and assessing what the individual was like before onset of the illness, and to what degree psychosocial functioning and developmental tasks were mastered before the individual became ill.

Successful psychosocial functioning comprises many components and is difficult to conceptualize and to define, especially in the form of a rating instrument. Further, it has not always been clear which aspects of premorbid life are most characteristic and have most predictive value in a rating scale. The most thoroughly studied premorbid scales, such as the Phillips Scale (Phillips 1953), the Elgin Prognostic Scale (Wittman 1941), the Premorbid Asocial Adjustment Scale (Gittelman-Klein and Klein 1969), and the Premorbid Adjustment Survey (Goldstein 1977), have shown poor premorbid adjustment to be related to various parameters including outcome of therapy, duration of hospitalization, and types of symptoms (Goldstein, Held, and Cromwell 1968; Klorman, Strauss, and Kokes 1977; Kokes, Strauss, and Klorman 1977). Most of these scales, however, were developed a number of years ago. Consequently, the items in many, while calling for subjective ratings, contain anchor points that no longer reflect cultural norms. Further, most scales fail to evaluate premorbid functioning

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systematically at several periods of life. The Premorbid Asocial Adjustment Scale (Gittelman-Klein and Klein 1969), which does incorporate continuity from one age level to another in some of its items, does not attempt to estimate function in adulthood. The Phillips Scale (Phillips 1953) addresses itself to sexual adjustment in adulthood long after the onset of sexual behaviors. The Kantor Scale (Kantor, Wallner, and Winder 1953), which also provides items for several periods of life from childhood through adulthood, was developed as a tool to dichotomize patients into process versus reactive schizophrenics. The scale does not provide items to measure developmental processes. It was noted by Houlihan (1977) that the process-reactive concept when implemented in a scale such as this tends to reflect the development of schizophrenic illness rather than the normal maturation process.

In the summer of 1977, the Center for Studies of Schizophrenia held a workshop focusing on difficulties in assessing premorbid adjustment (Keith and Buchsbaum 1978). The present scale was developed in response to suggestions and apparent consensus that came out of the workshop. We wished to develop a scale that (1) was useful for research purposes, (2) conceptualized successful premorbid adjustment in terms of the attainment of certain developmental goals that were viewed as necessary milestones for healthy functioning, and (3) considered attainment of these goals as specific age-related tasks. Thus, the individual with a poor premorbid adjustment was viewed as one who might not achieve one or more of these developmental goals before the onset of illness, or who might achieve them at a later period of life than is considered appropriate. Premorbid "competence," in social terms, could thus be measured by the extent to which the individual was able to meet age- and sex-appropriate expectations before becoming ill (Phillips 1953).

Description of the Scale

The Premorbid Adjustment Scale (PAS) (see Appendix) is a rating scale designed to evaluate the level of functioning in four major areas at each of several periods of the subject's life: social accessibility-isolation, peer relationships, ability to function outside the nuclear family, and capacity to form intimate socio-sexual ties. Items evaluating age-appropriate functioning in these areas are repeated for each period of the subject's life. The four life period sections are as follows: Childhood, up to 11 years; Early Adolescence, 12–15 years, Late Adolescence, 16–18 years; and Adulthood, 19 years and beyond. The final section, labeled General, is more global, containing items meant to estimate the highest level of functioning that the subject achieved before becoming ill, as well as the time span and characteristics of onset of illness, and general information such as amount of education. Scale items are made up of a combination of original, adopted, and modified items from the Phillips Scale, the Premorbid Social Adjustment Scale, and the Elgin Scale. The adopted items were chosen from these scales based on their suitability to each time period of the subject's life, and their suitability for estimating the successes and failures in the subject's development.

The scale is intended to measure only "premorbid" functioning, with "premorbid" being defined as the period ending 6 months before the first psychiatric hospital admission or psychiatric contact, or 6 months before evidence of characteristic florid psychotic symptomatology including delusions, hallucinations, thought disorder, inappropriate or bizarre behavior, or gross psychomotor behavior in which the symptoms are not apparently due to organic causes. Only those life periods that are premorbid by this definition should be rated on the scale, regardless of the present age of the subject; for example, a 39-year-old patient who had his first psychotic break at age 17 would not be rated in the adult section (age 19 and beyond), but would be rated on all the other scales, including the General section.

Ratings are based on histories derived from the subject's hospital records or family members. When it is felt that the patient is reliable, a personal interview may also be carried out to complete the ratings.

Rating. Each section of the scale contains a number of items with a scoring range of 0–6. The "0" end of the continuum denotes the hypothetically healthiest end of the adjustment range, and the "6" the hypothetically least healthy end. Descriptive phrases serve as rough anchor points. The rater selects the number that corresponds most closely to the descriptive phrase nearest it. Not every aspect included in a descriptive phrase is necessary for the rating. For example, "poor adaptation, dislikes school, frequent truancy, and frequent discipline problem" all appear opposite a rating of "4" on the school adaptation item. A child who has a poor adaptation to school, dislikes it, and is a discipline problem may be rated a "4," even though that child does not have a history of truancy. When the rater does not have sufficient information regarding a particular item, that item is not scored.

Scoring. The ratings received for each item in a section are summed and expressed as total score divided by the possible score. The possible score indicates the highest score obtainable by adding the maximum score for all items completed. Thus, if a subject receives ratings of 2, 3, 3, and 2 for the four items in the childhood section, the total score for that section is 10. The possible score is 24 (6+6+6+6), and the total score divided by the possible score is .42. When no information is available for a particular item, the item is not scored. The score for the section then is expressed as total score/possible score for the items rated. For example, if only three out of four of the items in the preceding example are scored, possible score becomes 18 (6+6+6) instead of 24. If the patient received the same ratings as in the previous example, except for one unratable last item, the total section score would be 8 (2+3+3). In this case, total score/possible score is 8/18 or .44.

An overall score for the whole scale may be calculated by averaging the subscale scores for all the subscales rated for the patient. An average is preferred to a total score in order to avoid bias that would occur in cases in which the sum of a few highly scored subscales would result in the same score as the sum of several moderately or low-scored subscales, when age of onset of illness or lack of information leads to some subscales being left out.

Reliability

Interrater reliability was determined in two studies. In the first study, two raters familiar with and experienced in the use of the PAS rated 11 patients. Both raters reviewed the patients' charts for psychosocial histories. In some instances, patient interviews were conducted with both raters present. After chart reviews and patient interviews were completed, the raters independently completed the PAS for each patient. The intraclass correlation coefficient for the two raters was $r = .85$ ($p = .0001$).

In the second study, interrater reliability among raters from another hospital who were unfamiliar with the scale and untrained in its use was investigated. Three raters at a California Veteran's Administration Hospital independently rated patients from chart histories alone. When these ratings were completed, the chart histories were reviewed by the two experienced raters. The intraclass correlation coefficient was $r = .40$ ($p = .01$) for the three Veteran's Administration Hospital raters and $r = .85$ ($p = .0001$) for the NIMH raters. The correlation for all five raters was .74 ($p = .0001$).

Table 1 contains intraclass correlation coefficients for each item and each subscale for all the raters. The correlations are statistically significant for all items except 5 and 6 in the General section.

Validity

Comparison With a Normal Population. A group of 76 normal controls (10 females and 66 males), made up of students, Air Force enlisted personnel, and employees of Saint Elizabeths Hospital, was rated on the PAS. Control subjects were told that the rating scale was being used to compare social development of "normal" persons with that of persons who had become mentally ill. The control subjects were interviewed by one of two raters who were familiar with the scale. The raters then filled out the PAS for the control subjects based on the information gathered in the interview. The mean ± standard error of the mean for each subscale and the Average score for the normals and for a group of 86 schizophrenic patients (12 females and 74 males) are shown in table 2. The patient population was from Saint Elizabeths Hospital and had volunteered to be a part of the study. All patients had met Research Diagnostic Criteria (Spitzer, Endicott, and Robins 1975) and Feighner Criteria (Feighner et al. 1972) for schizophrenia. The normals were significantly different ($p < .01$, two-tailed t test) on every subscale and on Average score from the patient population.

Outpatients vs. Chronically Hospitalized Patients. Patients were drawn from wards at Saint Elizabeths Hospital, Washington, D.C., or were outpatients from Saint Elizabeths. PAS ratings for the schizophrenic patients were accomplished by a combination of chart history review and personal interviews by the same raters who rated the normal subjects. All pa-

Table 1. Intraclass reliability coefficients for each item of the PAS for raters at Saint Elizabeths and the Palo Alto Veterans Administration Hospital

Subscale items	Saint Elizabeths		Subscales		VA hospital		Subscales		All raters		Subscales	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
C1	.92	.0000			.47	.796			.71	.0005		
C2	.75	.001			.50	1.0			.51	.009		
C3	.92	.0001			.13	.16			.67	.002		
C4	.70	—	.86	.000	−.48	.83	.53	.002	.36	.06	.62	.0000
EA1	.99	.0000			−.29	.47			.86	.0000		
EA2	.94	.0000			−.01	.24			.77	.0002		
EA3	.85	.0003			−.20	.38			.86	.0000		
EA4	.76	.002			.25	.12			.72	.0007		
EA5	.79	.003	.91	.0000	—	—	.16	.15	.80	.001	.83	.0000
LA1	.90	.001			.29	.10			.87	.0001		
LA2	.88	.0004			.41	.07			.78	.0004		
LA3	.91	.0004			−.33	.52			.87	.0001		
LA4	.37	.09			.17	.15			.39	.06		
LA5	.93	.0003	.87	.0000	−.20	.38	.53	.002	.93	.0000	.83	.0000
A1	.96	.001			−.33	.52			.92	.0001		
A2	.88	.003			.63	.03			.78	.001		
A3	.97	.0004	.96	.0000	.50	.05	.57	.006	.95	.0000	.91	.0000
G1	.88	.0001			−.31	.50			.69	.001		
G2	.56	.02			−.20	.38			.59	.005		
G3	.69	.003			−.11	.31			.52	.01		
G4	.86	.001			—	—			.94	.0000		
G5	.28	.13			—	—			.06	.28		
G6	.48	.03			−.46	.76			.15	.20		
G7	.73	.001			−.50	1.0			.73	.0004		
G8	.78	.001			—	—			.76	.0006		
G9	.86	.0006	.74	.0000	—	—	.34	.01	.79	.0008	.62	.0000
Full Scale			.85	.0000			.40	.0000			.74	.0000

C = Childhood; EA = Early Adolescence; LA = Late Adolescence; A = Adulthood; G = General.

tients' charts were reviewed, and interviews were conducted with patients who were well enough to cooperate. The majority of the patients were drawn from research wards, where care had been taken by the ward physicians and the psychiatric staff to acquire as full and detailed a history as possible for research purposes. Of the total group of 86 schizophrenic patients rated on the PAS, 19 were outpatients at the time the ratings were done. Approximately half of the remaining patients had been continuously hospitalized for 7 years or more. When we compared premorbid adjustment of the patients who were currently outpatients to that of the patients who had been continuously hospitalized for at least 7 years, the PAS successfully discriminated between the two groups. As expected, the patients who had been continuously hospitalized had significantly worse premorbid adjust-

Table 2. Means (± SEM) for normal controls and chronic schizophrenic patients on each subscale of the PAS and Average scale score

	Childhood		Early Adolescence		Late Adolescence		Adult		General		Average	
Subjects	Mean	*p*	Mean	*p*	Mean	*p*	Mean	*p*	Mean	*p*	Mean	*p*
Normal controls (*n*)	.23 (76)	.01	.21 (76)	.01	.17 (76)	.01	.12 (76)	.01	.09 (76)	.01	.16 (76)	.01
Schizophrenic patients (*n*)	.35 (77)	.02	.44 (76)	.02	.52 (61)	.02	.31 (32)	.02	.51 (86)	.02	.45 (86)	.02

ment scores. Significant discrimination was obtained for all subscales except Childhood (Early Adolescence, $p = .02$; Late Adolescence, $p = .009$; Adulthood, $p = .02$; and Average score, $p = .002$; one-way analysis of variance; table 3).

Length of Hospitalization. Reliable information regarding length of hospitalization was available for 39 patients. Average premorbid adjustment scores for these patients were correlated with the number of months of hospitalization (Pearson $r = .41$, $p = .006$). Chronic hospitalization was related to poor premorbid adjustment. When the individual subscale scores of the PAS were correlated with length of hospitalization, the Childhood ($r = .47$, $p = .003$), Early Adolescence ($r = .38$, $p = .03$), and General ($r = .36$, $p = .03$) subscales and Average scale ($r = .46$, $p = .005$) were significantly correlated (table 4).

Age of onset could be determined for 40 patients. These patients were divided by age of onset into four groups: age of onset of 15 years old and below (8 patients, mean ± SEM months hospitalization = 174 ± 54.3 months), 16 to 18 years old (18 patients, 109.7 ± 83.6 months), 19 to 24 years old (13 patients, 133.3 ± 46.3 months) and over 25 years old (1 patient, 216 months). The analysis of variance (ANOVA) between the groups for

Table 3. One-way ANOVA, mean ± SEM, and (*n*) for outpatients and inpatients on the subscales of the PAS

Subscales	Outpatients	Inpatients	*F*	*p*
Childhood	.37 ± .03 (17)	.45 ± .05 (19)	1.57	.22
Early Adolescence	.40 ± .04 (19)	.55 ± .05 (16)	5.98	.02
Late Adolescence	.46 ± .05 (18)	.67 ± .05 (11)	8.0	.009
Adulthood	.34 ± .05 (9)	.71 ± .08 (4)	18.1	.001
General	.44 ± .05 (20)	.59 ± .04 (20)	6.05	.02

Table 4. Length of hospitalization and premorbid adjustment

Subscale	Pearson *r*	*p*
Childhood	.47	.003
Early Adolescence	.38	.14
Late Adolescence	.28	.13
Adulthood	.56	.12
General	.36	.03
Average	.46	.005

length of hospitalization and age of onset was insignificant ($F = .60$, $p = .62$; see table 5). Table 6 provides item-by-item correlations for length of hospitalization.

Insidious vs. Acute Onset. Item number 3 in the General subscale assesses rapidity of onset of illness by change in work or school performance. Based on patients' scores on this item, we compared premorbid adjustment in patients who had an acute onset (defined as less than 3 months) to that of patients whose onset was rated as insidious (for whom it was rated difficult or impossible to determine the onset of deterioration). Twelve patients had been rated as having an acute onset of less than 3 months and 10 an insidious onset. The scale successfully discriminated between the two groups of patients on Average PAS and on all subscales except the Adult subscale (Childhood, $p = .004$; Early Adolescence, $p = .005$; Late Adolescence, $p = .005$; General $p = .0001$; Average, $p = .001$; one-way ANOVA; see table 7). Again, insidious onset was related to poor premorbid adjustment, while patients with an acute onset tended to have better premorbid adjustment.

Prediction of Subdiagnosis. Premorbid adjustment as measured by the PAS has been shown to be reasonably predictive of type of onset of illness, length of hospitalization, and need for continuous hospitalization for both the subscales and the Average score. The scale was less successful in predicting outcome for schizophrenic subcategories. Following confirmation of a schizophrenic diagnosis, the patients were further categorized as either chronic undifferentiated, paranoid, or chronic undifferentiated with paranoid features as determined by historical review, semistructured interview which included a Paranoid Dimension Checklist based on suggestions by David Rosenthal, and staff consensus on *DSM-II* categories (American Psychiatric Association 1968). A one-way ANOVA based on these subdiagnoses was significant for the diagnosis factor on the Late Adolescent ($p = .05$) and Adult ($p = .01$) subscales. Average score showed a tendency in the same di-

Table 5. One-way ANOVA by age of onset of subscales, Average score, and length of hospitalization: Means ± SEM and (*n*)

	Age of onset					
Variables	**15 or less**	**16–18**	**19–24**	**Over 25**	***F***	***p***
Childhood	.55 ± .01 (9)	.37 ± .04 (26)	.40 ± .04 (22)	.29 ± .06 (9)	2.75	.05
Early Adolescence	.54 ± .06 (4)	.46 ± .04 (27)	.44 ± .04 (24)	.36 ± .06 (10)	.99	.40
Late Adolescence	—	.54 ± .06 (16)	.54 ± .05 (25)	.42 ± .07 (10)	1.18	.32
Adulthood	—	—	.51 ± .07 (14)	.35 ± .05 (11)	3.53	.07
General	.70 ± .05 (9)	.46 ± .04 (27)	.49 ± .04 (26)	.36 ± .04 (12)	5.5	.002
Average	.63 ± .07 (9)	.45 ± .04 (27)	.46 ± .03 (26)	.35 ± .04 (12)	4.43	.007
Length of hospitalization (months)	174.9 ± 54.3 (8)	109.7 ± 19.7 (18)	133.5 ± 46.3 (13)	216 (1)	0.60	.62

Table 6. Correlations of individual PAS items with length of hospitalization

	Length of hospitalization	
Subscales	r	p
C1	.39	.02
C2	.48	.004
C3	.51	.004
C4	.40	.02
EA1	.36	.05
EA2	.52	.004
EA3	.41	.02
EA4	.32	.07
EA5	.33	.08
LA1	.24	.21
LA2	.22	.23
LA3	.50	.008
LA4	.24	.21
LA5	.19	.33
A1	.67	.10
A2	.60	.11
A3	.51	.16
G1	.39	.02
G2	.15	.38
G3	.18	.31
G4	.15	.40
G5	.05	−.80
G6	.29	.09
G7	.38	.03
G8	.42	.02
G9	.44	.01

Table 7. One-way ANOVA of type of onset of illness and PAS subscales, Average score, and Phillips score: Means ± SEM and (*n*)

Scales	Insidious	Acute	p
PAS Childhood	29 ± .05 (11)	60 ± .09 (9)	.004
PAS Early Adolescence	.31 ± .06 (12)	.63 ± .08 (8)	.005
PAS Late Adolescence	.35 ± .07 (9)	.70 ± .07 (6)	.005
PAS Adult	.27 ± .04 (5)	.57 ± .17 (3)	.06
PAS General	.29 ± .05 (13)	.74 ± .05 (10)	.000
PAS Average	.30 ± .05 (13)	.69 ± .06 (10)	.000
Phillips	22.9 ± 1.8 (12)	16 ± 3.0 (7)	.07

Table 8. Means (± SEM) for subdiagnostic groups on subscales of the PAS

Subscales	Paranoid	Chronic undifferentiated with paranoid features	Chronic undifferentiated
Childhood	.33 ± .03	.37 ± .07	.39 ± .04
Early Adolescence	.41 ± .03	.56 ± .09	.45 ± .04
Late Adolescence[1]	.44 ± .04	.64 ± .08	.57 ± .05
Adulthood[2]	.42 ± .06	.87 ± .07	.63 ± .09
General	.44 ± .03	.55 ± .06	.49 ± .04
Average[1]	.41 ± .03	.54 ± .06	.49 ± .04

[1] Significant at $p < .05$ on a one-way ANOVA based on subdiagnosis.

[2] Significant at $p < .01$ on a one-way ANOVA based on subdiagnosis. Newman-Keuls test indicated that the significant discriminations were due to the differences between paranoid and paranoid features groups.

rection ($p = .056$). (See table 8.) A Newman-Keuls test indicated that the difference between the paranoid and the paranoid features groups accounted for the significant discrimination in these subscales. The paranoid subgroup had the best premorbid adjustment of the three schizophrenic subgroups.

Relationship to Other Measures of Abnormality. Fifty-one of the chronic schizophrenic patients rated on the PAS also had computerized tomography (CT) scans done as part of a study that looked at brain abnormalities in chronic schizophrenia (Weinberger et al. 1980). Twenty-one patients had abnormal scans consisting primarily of enlarged lateral ventricles. Cortical atrophy was observed in three patients and atrophy of the anterior cerebellar vermis in two. The premorbid adjustment scores were significantly worse in the patients with abnormal CT scans compared with patients having normal scans, as measured on the Childhood ($p<.03$) and Early Adolescence ($p<.02$) subscales. Further, all patients who had severe maladjustment assessed by the Childhood subscale (rating over .50) had abnormal scans compared to 3 of 13 with normal scans (Fisher exact probability test, $p<.0001$). None of the patients were diagnosed as childhood schizophrenics.

Comparison of the PAS and the Phillips Scale. One of the most widely used premorbid adjustment scales is the Premorbid History section of the Phillips Prognostic Rating Scale. Twenty patients rated on the PAS were also rated on the Premorbid History part of the Phillips Scale in order to compare the PAS with the most standard scale currently in use. In table 9 correlations of the PAS (subscales and Average scores) and Phillips Scale scores are presented for length of hospitalization and age of onset of illness. Correlations are presented for the total PAS population for whom these data were available and for the subgroup who were rated on the Phillips. For the total PAS population, the Childhood, Early Adolescence, and General subscales of the PAS and the Average PAS score correlate significantly with length of hospitalization compared with r = 20 (p = .46) for the

Table 9. Correlation coefficients (*rho*) of length of hospitalization and age of onset of illness for PAS subscales, Average score, and Phillips score

	Length of hospitalization				Age of onset			
	Total population		Patients rated on Phillips		Total population		Patients rated on Phillips	
Scales	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
PAS Childhood	.47 (37)	.003	.48 (16)	.06	−.20 (59)	.14	.10 (17)	.69
PAS Early Adolescence	.38 (34)	.03	.14 (15)	.61	−.28 (60)	.03	−.32 (17)	.20
PAS Late Adolescence	.28 (31)	.13	.17 (14)	.56	−.34 (55)	.01	−.37 (16)	.16
PAS Adulthood	.56 (9)	.12	.70 (4)	.29	−.36 (23)	.09	−.75 (5)	.15
PAS General	.36 (37)	.03	.29 (16)	.26	−.31 (66)	.01	−.27 (18)	.28
PAS Average	.46 (37)	.005	.30 (16)	.26	−.35 (66)	.004	−.14 (18)	.58
Phillips	.20 (16)	.46	.20 (16)	.46	−.31 (18)	.21	−.31 (18)	.21

Correlations are presented for the full PAS population and for the subpopulation of patients also rated on the Phillips. Number of subjects denoted by (n).

Phillips. Age of onset showed an inverse significant correlation with Early Adolescence, Late Adolescence, General, and Average PAS scores. The correlation between the age of onset and the Phillips score ($r = .31$, $p = .21$) is not significant. Correlations calculated for only those patients who were also rated on the Phillips Scale are, in most instances, lower and do not reach significance, as might be expected with a small sample. However, correlations between length of hospitalization and Childhood, Adulthood, and General subscale scores and Average score on the smaller PAS population remain higher than the correlation between the Phillips score and length of hospitalization, and approach significance on the Childhood subscale. The PAS did about as well as the Phillips in the case of correlations between age of onset and premorbid ratings in the subpopulation.

Information on type of onset of illness (insidious or acute) was available for 19 of the 20 patients rated on the Phillips Scale. The mean Phillips scores for patients with insidious versus acute onset of illness were 22.7 ± 1.8 and 16 ± 3.0, respectively. The difference was not significant. The PAS differences in type of onset are significant (table 6).

Typically, a rating of "3" on the Phillips Scale has been taken as the dividing point for predicting good and poor outcome (Kokes, Strauss, and Klorman 1977). When this criterion was used, patients for whom CT scan information was available were divided into "poor" and "good" premorbid groups and "normal" or "abnormal" CT scan groups (Weinberger et al. 1980). A Fisher exact probability statistic was computed and was not significant ($p = .77$), indicating that premorbid adjustment as measured by the Phillips and dichotomized in this way does not differentiate between patients with "normal" and "abnormal" CT scans as does the PAS. Weinberger et al. compared patients with "normal" and "abnormal" CT scans using the Childhood subscale of the PAS. Of nine patients with poor childhood adjustment (rating of more than .50) all had abnormal scans, whereas only 3 of the 13 who had good childhood adjustment (rating less than .20) had abnormal scans (Fisher exact probability, $p < .001$).

Comment

The Premorbid Adjustment Scale (PAS) was devised primarily to measure the degree of success in attainment of certain developmental goals at each phase of a subject's life. Social isolation was felt to be one of the clear-cut signs of a poor premorbid adjustment, particularly if present in Late Adolescence. The capacity to make intimate sexual attachments with others and the ability to function successfully away from home (in school, for instance) were felt to be vital. Items dealing with these aspects of premorbid functioning were thus assessed in each life period by the appropriate subscale. Emphasis was placed largely on asocial characteristics of social functioning; however, some items in the scale (the school adjustment items) tap antisocial behavior as well. It has been suggested that asocial premorbid adjustment may characterize a different type of outcome than does antisocial premorbid adjustment—that is, that individuals who act out against society develop different kinds of mental problems than do people who withdraw from society (Quitkin, Rifkin, and Klein 1976). The PAS in its present form cannot discriminate between these different types of individuals.

More data are needed and are currently being collected regarding the influence, if any, on scale scores of gender, socioeconomic level, and race. We are also studying premorbid adjustment in acute schizophrenic patients.

One of the most widely used premorbid adjustment scales is the Premorbid History section of the Phillips Prognostic Rating Scale. The PAS was significantly correlated with length of hospitalization (Childhood, Early Adolescence, and General subscales, and Average PAS score), while the Phillips was not. An inverse correlation with age of onset also distinguished the scales, where high scores on the PAS in Early Adolescence, Late Adolescence, and General subscales were related to early onset of illness, but age of onset was not significantly correlated with the Phillips scores. If only the PAS scores for the subpopulation of patients who were also rated on the Phillips are used, the PAS performed overall as well as or better than the Phillips Scale in correlating premorbid adjustment with length of hospitalization and age of onset. Further, type of onset of illness was differentiated by the PAS on all but the Adult subscales but not by the Phillips. The Phillips did not distinguish between patients with normal and abnormal CT scans. The majority of the patients rated on the Phillips Scale had high total scores of 20 points or more (14 of 20 patients, range, 10–29). The PAS data provided a broader spread of scores, from low (healthier) to high (less healthy) (range .03–.99), as well as availability of several subscales, which may partially account for its finer apparent discriminative capability.

In examining the discriminative ability of the subscales to predict length of hospitalization or type of onset, we were concerned that premorbid functioning scores might have been contaminated by age of onset of illness, leading to comparisons, for example, in which 80 of 86 patients were compared on the Childhood subscale with 5 of 86 patients on the Adult subscale because patients were not rated on a subscale after the onset of illness. To address this concern, we grouped patients according to age of onset of illness (15 years or younger, 16–18, 19–24, and over 25) and compared the mean PAS scores for each subscale by a one-way ANOVA (table 5). No significant differences in PAS scores for the Early Adolescence, Late Adolescence, and Adulthood subscales were found. Age of onset was not related to length of hospitalization. The group which became ill at 15 years of age or younger did have significantly worse premorbid adjustment scores in the Childhood subscale ($p = .05$). (A Newman-Keuls test indicated that the significance was accounted for by the difference between the 15 year or younger group and the 25 or older group.) A significant relationship was also found for the General subscale and for the Average score. The significant F ratios for these findings are attributable to the differences between the 15 year or younger onset group and the other three age of onset groups (Newman-Keuls test). No significant differences on the Newman-Keuls test were found between the 16–18, 19–24, and 25 and over age of onset groups for these measures. In the age of onset at 15 years or younger group, three of the nine patients in the group became ill at 15, two at 14, two at 13, and two at age 12. Those patients with onset of illness at 15 years or younger have worse childhood adjustment than those with onset of illness at 16 years of age or older. In spite of the lack of statistical evidence for an association between age of onset and PAS scores in age groups other than the 15 and below age group, it would be unwise to assume that age of onset may be safely disregarded when interpreting the relationship between the PAS and other variables—length of illness, for example. This is particularly problematic in cases of insidious onset of illness when the likelihood that the scale is measuring early morbid rather than premorbid functioning is increased. It is recommended that investigators acquire as full and complete a history as possible, and where age of onset is difficult to pinpoint, a conservative approach with regard to whether or not to rate a patient on a particular subscale should be adopted.

When patients with normal and abnormal CT scans were compared, all nine patients with severe social maladjustment in childhood had abnormal scans. Weinberger et al. (1980) suggest that CT scan abnormalities in schizophrenia relate to a pathological process occurring early in development. The PAS appears to be capable of detecting the social aspects of that process. These data support the usefulness of a developmental approach to measuring premorbid adjustment.

Interrater reliability for untrained raters, using patients' charts, while adequate, was not nearly so good as that for trained raters. This may represent a disadvantage for the researcher or clinician who would like to use the scale as a quick estimate of premorbid adjustment. Best quality data will require training of raters.

The advantages of the scale lie in its simplicity and its adaptability to a variety of information sources. It can be rated on the basis of personal interviews, family informants, or chart histories, and is therefore of value for a variety of research purposes. It is useful in identifying patients likely to become chronically hospitalized or at high risk for readmission. It may also serve as a possible predictor of patients with brain abnormalities on CT scan.

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Appendix: Premorbid Adjustment Scale

Childhood (up through age 11)

1. Sociability and withdrawal

0 Not withdrawn, actively and frequently seeks out social contacts.
1
2 Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize.
3
4 Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others but does not seek it.
5
6 Unrelated to others, withdrawn and isolated. Avoids contacts.

2. Peer relationships

0 Many friends, close relationships with several.
1
2 Close relationships with a few friends (one or two), casual friendships with others.
3
4 Deviant friendship patterns: friendly with children younger or older only, or relatives only, or casual relationships only.
5
6 Social isolate, no friends, not even superficial relationships.

3. Scholastic performance

0 Excellent student.
1
2 Good student.
3

4 Fair student.

5

6 Failing all classes.

4. Adaptation to school

0 Good adaptation, enjoys school, no or rare discipline problems, has friends at school, likes most teachers.

1

2 Fair adaptation, occasional discipline problem, not very interested in school, but no truancy, or rare. Has friends in school, but does not often take part in extracurricular activities.

3

4 Poor adaptation, dislikes school, frequent truancy, frequent discipline problem.

5

6 Refuses to have anything to do with school—delinquency or vandalism directed against school.

Adolescence (Early, ages 12–15)

1. Sociability and withdrawal

0 Not withdrawn.

1

2 Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize.

3

4 Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others, but does not seek it.

5

6 Unrelated to others, withdrawn and isolated. Avoids contact.

2. Peer relationships

0 Many friends, close relationships with several.

1

2 Close relationships with a few friends (one or two), casual friendships with others.

3

4 Deviant friendship patterns: friendly with children younger or older only, or relatives only, or casual relationships only.

5

6 Social isolate, no friends, not even superficial relationships.

3. Scholastic performance

0 Excellent student.

1

2 Good student.

3

4 Fair student.

5

6 Failing all classes.

4. Adaptation to school

0 Good adaptation, enjoys school, no or rare discipline problems, has friends at school, likes most teachers.

1

2 Fair adaptation, occasional discipline problem, not very interested in school, but no truancy, or rare. Has friends in school, but does not often take part in extracurricular activities.

3

4 Poor adaptation, dislikes school, frequent truancy, frequent discipline problem.

5

6 Refuses to have anything to do with school—delinquency or vandalism directed against school.

5. Social-sexual aspects of life during early adolescence

0 Started dating, showed a "healthy interest" in the opposite sex, may have gone "steady," may include some sexual activity.

1 Attachment and interest in others, may be same-sex attachments, may be a member of a group, interested in the opposite sex, although may not have close, emotional relationship with someone of the opposite sex, "crushes" and flirtations.

2 Consistent deep interest in same-sex attachments with restricted or no interest in the opposite sex.

3 Casual same-sex attachments, with inadequate attempts at relationships with the opposite sex. Casual contacts with both sexes.

4 Casual contacts with the same sex, no interest in the opposite sex.

5 A loner, no or rare contacts with either boys or girls.

6 Antisocial, avoids and avoided by peers. (Differs from above in that an active avoidance of others rather than passive withdrawal is implied.)

Adolescence (Late, ages 16–18)

1. Sociability and withdrawal

0 Not withdrawn.

1

2 Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize.

3

4 Moderately withdrawn, given to daydreaming and exces-

sive fantasy, may passively allow self to be drawn into contact with others, but does not seek it.

5

6 Unrelated to others, withdrawn and isolated. Avoids contact.

2. Peer relationships

0 Many friends, close relationships with several.

1

2 Close relationships with a few friends (one or two), casual friendships with others.

3

4 Deviant friendship patterns: friendly with children younger or older only, or relatives only, or casual relationships only.

5

6 Social isolate, no friends, not even superficial relationships.

3. Scholastic performance

0 Excellent student.

1

2 Good student.

3

4 Fair student.

5

6 Failing all classes.

4. Adaptation to school

0 Good adaptation, enjoys school, no or rare discipline problems, has friends at school, likes most teachers.

1

2 Fair adaptation, occasional discipline problem, not very interested in school, but no truancy, or rare. Has friends in school, but does not often take part in extracurricular activities.

3

4 Poor adaptation, dislikes school, frequent truancy, frequent discipline problem.

5

6 Refuses to have anything to do with school—delinquency or vandalism directed against school.

5. Social aspects of sexual life during adolescence and immediately beyond

0 Always showed a "healthy interest" in the opposite sex, dating, has gone "steady," engaged in some sexual activity (not necessarily intercourse).

1 Dated regularly. Had only one friend of the opposite sex with whom the patient went "steady" for a long time. (Includes sexual aspects of a relationship, although not necessarily intercourse; implies a twosome, pairing off into couples, as distinguished from below.)

2 Always mixed closely with boys and girls. (Involves membership in a crowd, interest in and attachment to others, no couples.)

3 Consistent deep interest in same-sex attachments with restricted or no interest in the opposite sex.

4 Casual same-sex attachments with inadequate attempts at adjustment to going out with the opposite sex. Casual contacts with boys and girls.

5 Casual contacts with same sex with lack of interest in opposite sex. Occasional contacts with the opposite sex.

6 No desire to be with boys and girls, never went out with opposite sex.

Adulthood (Age 19 and above)

1. Sociability and withdrawal

0 Not withdrawn, actively and frequently seeks out social contact.

1

2 Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize.

3

4 Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others but does not seek it.

5

6 Unrelated to others, withdrawn and isolated. Avoids contacts.

2. Peer relationships

0 Many friends, close relationships with several.

1

2 Close relationships with a few friends (one or two), casual friendships with others.

3

4 Deviant friendship patterns: friendly with children younger or older only, or relatives only, or casual relationships only.

5

6 Social isolate, no friends, not even superficial relationships.

3. Aspects of adult social-sexual life.

a. Married, presently or formerly:

0 Married, only one marriage (or remarried as a result of death

of spouse), living as a unit, adequate sexual relations.

1 Currently married with history of low sexual drive, periods of difficult sexual relations, or extramarital affair.

1 Married, more than one time, currently remarried. Adequate sexual relations during at least one marriage.

2 Married, or divorced and remarried, with chronically inadequate sex life.

2 Married, and apparently permanently separated or divorced without remarriage, but maintained a home in one marriage for at least 3 years.

3 Same as above, but: divorce occurred over 3 years ago, and, while married, maintained a home for less than 3 years.

b. Never married, over 30:

2 Has been engaged one or more times or has had a long-term relationship (at least 2 years) involving heterosexual or homosexual relations, or apparent evidence of a love affair with one person, but unable to achieve a long-term commitment such as marriage.

3 Long-term heterosexual or homosexual relationship lasting over 6 months but less than 2 years. (If stable, long-lasting homosexual relationship, over 2 years, score as "3.")

4 Brief, or short-term dating experiences (heterosexual or homosexual) with one or more partners, but no long-lasting sexual experience with a single partner.

5 Sexual and/or social relationships rare or infrequent.

6 Minimal sexual or social interest in either men or women, isolated.

c. Never married, age 20–29:

0 Has had at least one long-term love affair (minimum of 6 months) or engagement, even though religious or other prohibitions or inhibitions may have prevented actual sexual union. May have lived together.

1 Has dated actively, had several "boyfriends" or "girlfriends," some relationships have lasted a few months, but no long-term relationships. Relationships may have been "serious," but a long-term commitment such as marriage was not understood to be an eventuality.

3 Brief, short-term dating experiences or "affairs" with one or more partners, but no long-lasting sexual experiences with a single partner.

4 Casual sexual or social relationships with persons of either sex with no deep emotional bonds.

5 Sexual and/or social relationships rare or infrequent.

6 Minimal sexual or social interest in either men or women, isolated.

General

1. Education

0 Completed college and/or graduate school, or professional school (Law, for example).

1 Completed high school and some college or vocational training school or business school (such as secretarial or computer programming schools).

2 Completed high school.

3

4 Completed eighth grade.

5

6 Did not get beyond fifth grade.

2. During a period of 3 years up to 6 months before first hospitalization or onset of first episode, patient was employed for pay or functioning in school

0 All the time.

1

2 Half the time.

3

4 Briefly, about 25 percent of the time.

5

6 Never.

3. Within a period of a year up to 6 months before first hospitalization or first episode change in work or school performance occurred

0 Abruptly.

1

2 Within 3 months.

3

4 Within 6 months.

5

6 Imperceptibly, difficult or not possible to determine onset of deterioration.

4. During a period of 3 years up to 6 months before first hospitalization or first episode, frequency of job change, if working, or interruption of school attendance was

0 Same job held, or remained in school.

1

2 Job change or school interruption occurred two to three times.

3

4 Kept the same job more than 8 months but less than a year, or remained continuously in school for the same period.

5

6 Less than 2 weeks at a job or in school.

5. Establishment of independence

0 Successfully established residence away from family home, financially independent of parents.

2 Made unsuccessful attempts to establish independent residence, lives in parents' home, but pays parents room and board, otherwise financially independent.

4 Lives in parents' home, receiving an allowance from parents which patient budgets to pay for entertainment, clothes, etc.

6 Made no attempt to leave home or be financially independent.

6. Global assessment of highest level of functioning achieved in patient's life

0 Fully able to function successfully in and take pleasure from (1) school or job; (2) friends; (3) intimate sexual relationships; (4) church, hobbies, etc. Enjoys life and copes with it well.

2 Able to function well in and enjoys some spheres of life, but has a definite lack of success in at least one area.

4 Minimum success and pleasure in three areas of life.

6 Unable to function in or enjoy any aspect of life.

7. Social-personal adjustment

0 A leader or officer in formally designated groups, clubs, organizations, or athletic teams in senior high school, vocational school, college, or young adulthood. Involved in intimate, close relationship with others.

1 An active and interested participant, but did not play a leading role in groups of friends, clubs, organizations, or athletic teams, but was involved in close relationships with others also.

2 A nominal member, but had no involvement in or commitment to, groups of friends, clubs, organizations, etc. Had close relationships with a few friends.

3 From adolescence through early adulthood had a few casual friends.

4 From adolescence through early adulthood had no real friends, only superficial relationships.

5 From adolescence through early adulthood (i.e., after childhood), quiet, seclusive, preferred to be by self, minimal efforts to maintain any contact at all with others.

6 No desire to be with peers or others. Either asocial or antisocial.

8. Degree of interest in life

0 Keen, ambitious interest in some of the following: home, family, friends, work, sports, art, pets, gardening, social activities, music, and drama.

2 Moderate degree of interest in several activities including social gatherings, sports, music, and opposite sex.

4 Mild interest in a few things such as job, family, quiet social gatherings. The interest is barely sustaining.

6 Withdrawn and indifferent toward life interests of average individual. No deep interests of any sort.

9. Energy level

0 Strong drive, keen, active, alert interest in life. Liked life and had energy enough to enjoy it. Outgoing and adequate in meeting life.

2 Moderately adequate drive, energy, interest, as described above.

4 Moderately inadequate energy level. Tended toward submissive, passive reactions. Showed some potential to face life's problems, but would rather avoid them than expend the necessary energy.

6 Submissive, inadequate, passive reactions. Weak grasp on life, does not go out to meet life's problems, does not participate actively, but passively accepts his lot without having the energy to help self.

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Documenting an Episode of Psychiatric Illness: Need for Multiple Information Sources, Multiple Raters, and Narrative

by Ian F. Brockington and Herbert Y. Meltzer

Abstract

It is argued that the structured psychiatric interview, which has become the foundation of much modern clinical research, is not a sufficient method of documenting an episode of psychotic illness. This valuable resource needs to be supplemented by a high standard of recorded observation throughout hospitalization by all staff in contact with the patient. The conversion of observations into ratings can involve considerable error and should be left to at least two highly trained research workers. The only data worthy of this effort are the entire body of clinical information obtained from all sources. This requires detailed written records. The advantage of a narrative record, in addition to numerical ratings, is that it can be reinterpreted at any time using different systems of psychopathological or nosological ideas.

Documenting the signs and symptoms of a psychotic episode is often difficult because of the nature of the material. The subject matter consists of mental experiences and altered behavior—phenomena that are inherently difficult to comprehend, measure, and describe. When ascertaining the symptoms, the observer is at the mercy of the patient's own perceptual and descriptive limitations, aggravated by mental illness, while behavioral events are transitory, unpredictable, and hard to scrutinize. Clinical data, therefore, are liable to be riddled with inaccuracy, greatly increasing the difficulty of all research which involves dividing patients into groups, or measuring the change of state. In some disciplines, such as epidemiology, it is possible to compensate for observational error by large numbers, but it is often necessary to manage with small samples, especially now that psychiatrists are narrowing their focus and trying to draw finer distinctions between psychotic states. For such studies it is important to develop clinical techniques which are precise and sensitive, documenting the phenomena with minimum error. This article addresses the questions of how clinical psychiatric research should be conducted in order to obtain a more complete and accurate picture of a psychotic episode.

The Need for Multiple Information Sources

The Structured Psychiatric Interview. The structured interview is the mainstay of modern clinical study. The principles of interviewing are well understood. The interviewer prepares by reading the case records before seeing the patient, forms a relationship with him explaining the purpose of the interview, allows time for his spontaneous complaints before proceeding to direct questioning, uses the interview flexibly but asks all the recommended probes, avoids leading questions, cross-examines and clarifies the nature of the symptoms, and never accepts the presence of a phenomenon unless it is clearly described in the patient's own words. After the interview, he completes a set of ratings aided by a glossary. This

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form of inquiry has been developed to a high level at the New York State Psychiatric Institute (Spitzer et al. 1970) and the M.R.C. Social Psychiatry Unit in London (Wing, Cooper, and Sartorius 1974), but there is a danger that its use will lead to complacency and overconfidence, giving investigators a false sense of the thoroughness, reliability, and validity of their clinical assessment. It should provide a comprehensive inventory of recent symptoms provided that the patient is capable of giving a clear account—a condition not met in about 25 percent of psychoses (Brockington and Leff 1979). The behavioral observations are less likely to be representative of the whole episode because of the brevity of the contact between observer and patient. When the aim is to document an episode lasting weeks or months, a single 1-hour interview, however thorough the observer's methodology and training, is not a sufficient source, and its limitations have been shown by measurements of its test-retest reliability and validity. Some test-retest reliabilities, taken from studies of the 7th and 8th editions of the Present State Examination (Wing et al. 1967; Kendell et al. 1968), the Psychiatric Status Schedule (Spitzer et al. 1970), the Schedule for Affective Disorders and Schizophrenia (Endicott and Spitzer 1978), and the International Pilot Study of Schizophrenia (IPSS) (World Health Organization 1973), are shown in table 1. Reliability improves as one moves from items to section scores and syndromes. At the level of syndromes—called "groups of units of analysis" in the IPSS—or diagnoses, it is good, but for items it is poor. The reasons for the discrepancies are unclear. They may be due to variations in interview administration or scoring which could be removed by further standardization and training. Alternatively they may be due to variation in the patient's description of his symptoms; he may be reporting his state of mind on a particular day or in the immediate past and not during the last month or the whole episode. Whatever the reason, the test-retest reliability measurements suggest that only the broad outlines of an episode are agreed upon in two interviews held a few days apart. When the aim is to find distinctions between psychotic states, it is not likely that broad outlines will provide the answer. For example, the distinction between bipolar and other depressive illnesses at present depends mainly on the occurrence of manic episodes, because we cannot reliably distinguish manic-depressive disease in its depressed form from unipolar depressive disorder. When searching for psychopathological differences between bipolar and nonbipolar depression, it is probable that detailed symptomatology—for example, the severity of retardation, the worsening of symptoms in the morning, the lack of anxiety, and the presence of particular kinds of delusion—will prove discriminating, rather than overall section scores. It is necessary, therefore, to achieve satisfactory reliability at the item level.

There have, to our knowledge, been only two attempts to study the validity of the psychiatric interview by comparing it with a criterion that was at least partly independent and based on a larger body of data. Carpenter et al. (1976) compared interview ratings with those made by the psychiatrist-in-charge after a month's observation. The interview ratings were unseen, but the clinician attended the research interview. They found that the interview missed 30 percent of the psychopathology which later became evident. Downing, Francis, and Brockington (1980) compared five information sources with a criterion. The sources comprised a psy-

Table 1. Test-retest reliability of the psychiatric interview

Ratings	Interview	Statistic	Value
Interview behavior	PSE (7th)	K_w (mean)	.37
	St. Louis[1]	K (mean)	.36
Symptoms	PSE (7th)	K_w (mean)	.41
	St. Louis	K (mean)	.55
Section scores	PSE (7th)	r (mean)	.55
	PSE (8th)	r (mean)	.49
	IPSS	r (median)	.45
	PSS	r (median)	.57
Syndromes	IPSS	r (median)	.60
	SADS	r (median)	.83
Diagnosis	St. Louis	K (mean)	.66

K = Cohen's Kappa; K_w = weighted Kappa; *r* = intraclass correlation coefficient.

[1] Helzer et al. (1978).

chiatric interview, interview with a relative, nurse rating, self-rating and brief videotaped interview. The criterion was a set of "master ratings" made by three observers reviewing all the research data (except self-ratings) and the hospital records. It was independent of the self-ratings but not independent of the other sources, which contributed to varying extents. The psychiatric interview contributed about 20 percent (800 words) of the information available, but in terms of detailed verbatim replies to key questions, its contribution was greater. In spite of this, it missed over half the items agreed to be present, and there was an overall underrating of the severity of phenomena. Some of its deficiencies are listed in tables 2 and 3.

Multiple Research Interviews. To supplement the psychiatric interview, the first resource is the use of several interviews. It is good practice to conduct the initial interview in two stages. The first is done shortly after admission and has the purpose of establishing rapport, observing the patient's state when most severely disturbed, recording his complaints, and checking his cognitive function. The second is done a day or two later to make a second set of behavioral observations, assess the persistence of the main symptoms, and complete the routine probes. Two shorter interviews make fewer demands on both patient and interviewer. A psychiatric interview is demanding because the observer is involved simultaneously in several different roles: He has to maintain a professional relationship with the patient, treating him with respect and concern, and giving him scope to express his preoccupations; he has to control the dialogue and ensure that every area is explored; he has to evaluate the symptomatology, matching the patient's description against the glossary; and he has to switch into an objective stance when rating affect, speech, and behavior.

In addition to the initial interviews, it seems of value to conduct a full structured interview at the time of discharge. The patient may then be able to describe experi-

Table 2. Some low concordances between psychiatric ratings and master ratings

Items	Item rated in psychiatric interview	Items agreed to be present	Kappa
Agitation	3	20	.14
Excitement and violence	2	14	.19
Perplexity	2	12	.23[1]
Incongruous affect	6	17	.38[2]
Lability of mood	5	15	.41[1]
Guilt	10	23	.41[2]
Visual hallucinations	4	12	.43[2]
Denial of abnormality	10	21	.43[2]
Panic attacks	3	8	.44[2]

[1] $p<.05$.
[2] $p<.01$.

Table 3. Some low correlations between psychiatric ratings and master ratings

Scales	Mean score from psychiatric interview	Mean score from master ratings	Pearson's *r*
Concern for others	18	30	.03
Incompetence	21	44	.05
Social withdrawal	17	29	.23
Manipulative behavior	8	9	.23
Uncooperative behavior	13	30	.31[1]
Self-neglect	10	13	.49[2]
Confusion	7	18	.51[2]
Worrying	20	33	.53[2]
Somatic concern	11	20	.59[2]

[1] $p<.05$.
[2] $p<.01$.

ences still recent and vividly remembered which he could not clearly describe on admission because of guarding, muteness, or incoherence. The time of discharge is an opportunity to assess the degree of recovery, which is considered one of the most important variables in making a diagnosis. Once the patient has left the hospital it may be difficult to trace and interview him again.

Case Records. Research records can be supplemented by interviews recorded in the case notes (charts). These are held throughout the period of hospitalization and record the course of the episode. The information has been gathered without the discipline of the formal research interview, but is not thereby invalidated. All trainee psychiatrists can be trained in the method of interviewing, which is simpler than training them in the practice of rating. If they are taught to record phenomena in plain language rather than professional jargon—to refrain from converting their observations into inferential terms whose definitions vary from time to time and from center to center (e.g., delusions, thought disorder, blunting of affect) and report what was said and what they saw—their information would have the same value as the research interview, lacking only the range of the full inventory. The limitations would be set by their personal observational and writing skills rather than the formality of the method. In some centers (e.g., the Professorial Unit at the Maudsley Hospital) a high standard of recordkeeping has been maintained for many years, and it is possible to use these data for nosological research (e.g., Cutting, Clare, and Mann 1978). In the study of the longitudinal course of psychotic illness, the general quality of hospital notes is a limiting factor since few of the episodes can be studied by a research team.

Interviews With Other Informants. So far this article has addressed what can be learned by interviewing the patient. The particular value of interviewing a close relative or cohabitee is that his frame of reference includes the patient's normal personality and he can report the contrast between it and the present state. He can give an objective account of the historic development of the episode and of major events preceding admission such as suicide attempts. Relatives can be interviewed in a high percentage of cases—88 percent in the study of Downing, Francis, and Brockington (1980). One can use a structured interview similar to that used to interview the patient, with slightly modified probes. Downing, Francis, and Brockington (1980) found highly significant correlations between ratings made from this interview and master ratings in 25/57 areas studied. There were only five areas in which they were much better than those based on the psychiatric interview—social withdrawal, increased sociability, incompetence, euphoria, and increased energy. Three of these are useful in the diagnosis of mania. Like the psychiatric interview this source underestimated the severity of psychopathology in every area except anxiety and poverty of contact, and correctly identified only 38 percent of the items agreed to be present.

Nurse Ratings. After the patient's hospital admission, members of the nursing staff take over the relatives' role in relating to the patient in almost all the circumstances of his daily life. As Bunney and Hamburg (1963) have pointed out, nurses are in a unique position, having a well-accepted place on the unit, having direct contact with the patient in the course of their regular duties, and being able to make a continuous series of observations throughout the day and night. They observe the patient in the washroom, at meal times, and relating to other patients, to staff of all kinds, and to relatives, in group meetings, and (especially if occupational therapists are drawn in) when engaged in a wide range of activities. They are able to assess the variability or persistence of affective symptoms and the frequency of abnormal behaviors, and can provide evidence for an assessment of orientation and volition. To varying extents they lack a precise glossary of terms, but they do not lack experience of psychotic phenomena. Their evidence is indispensable and is the only source always available once the patient has been hospitalized.

Downing, Francis, and Brockington (1980) studied the validity of nurses' ratings, compared with the comprehensive criterion described above. They found that ratings made after a single 8-hour shift correctly identified only 24 percent of the items agreed to be present during the whole episode, but that nurses' ratings were in agreement with master ratings at the 1 percent level of significance in 29/57 areas studied. The highest correlations were all concerned with behavior (retardation, loss of reserve, poverty of contact, social withdrawal, concern for others, disorganized communication, incompetence, and uncooperative behavior with Pearson's *r* in the range .58–.64), but there were fairly high correlations in some symptom areas too, including guilt ($r = .58$), hypochondriasis ($r = .57$), delusions ($r = .53$), and auditory hallucinations ($r = .54$). In four areas nurses' ratings had the best agreement with the criterion of all the sources studied—namely, uncooperative behavior, concern for others, agitation, and distractibility.

Since the introduction of ward behavior charts at the Phipps Clinic in Baltimore (Kempf 1915), a great many nurses' rating scales and schedules have been published. One of the main problems is that nurses are less highly trained than psychiatrists and psychologists in rating psychopathology and some reports on their reliability have been adverse (Jensen and Morris 1960; Downing and Brockington 1978). In the writers' view, the advantages of nursing observations are lost if they are all converted to ratings. The virtue of the nursing input is that it comes from a multitude of personnel working continuously with the patient. One cannot expect them all to maintain a high standard of rating, but one can expect them to report what happens. They are already accustomed to writing regular transfer notes, which provide useful data on day-to-day change and salient incidents. For research purposes it is necessary to train nurses to describe their observations in a more detailed and graphic form. The process of sharpening observational skills and improving communication will have a beneficial effect on nursing, as well as furnishing a prime source of information.

Self-Report. In theory the patient's own account of his psychosis has a special interest and value. In practice few patients provide an unstructured account of their experiences and ideas, and a good psychiatric interview records the main symptoms verbatim. Self-diagnosis and self-ratings made by the patient have many disadvantages; the patient has no frame of reference outside his own experience, and his answers may be distorted by dissimulation or other forms of response bias. In nosological studies, however, self-rating has the advantage of being free from the observers' theoretical prejudices, whose effects on perception, reporting, and rating are hard to eliminate. In the patient's own ratings we have a source completely purged of this subtle and pervasive distortion.

In the Manchester study (Downing, Francis, and Brockington 1980), some observations on self-rating were made using a set of 100 questions about the current mental state to be answered "yes" or "no" by forced choice. Forty-six out of 50 patients were able to complete this procedure. From the replies, 22 scales were arbitrarily constructed, corresponding to the master rating scales. It was found that eight of them had significant correlations ($p = < .001$) with the master ratings. They comprised elation ($r = .61$), hopelessness ($r = .54$), guilt ($r = .52$), auditory hallucinations ($r = .51$), grandiosity ($r = .50$), social withdrawal ($r = .49$), insomnia ($r = .46$), and sadness ($r = .44$). The correlations were modest, but the criterion was entirely independent. When used in an empirical study of the difference between puerperal and nonpuerperal depression (Brockington et al., unpublished data), the self-ratings yielded an unexpected and valuable finding completely missed by observer ratings. It was not possible by observer ratings to distinguish between the severity of depression in the two groups, but self-ratings of sadness showed a marked difference, with puerperal depressions having significantly lower scores ($p = .005$). Thus in a broad approach to the sudy of mental state, self-ratings may have a limited but useful contribution to make.

Recorded Interviews. The development of videotape recordings has made it possible to make a permanent replica of interactions with patients, which has many advantages over the written record. The interview can be studied repeatedly by the most experienced raters, and difficult judgments about affect (e.g., perplexity and blunting) can be made by experts. It can be studied at leisure by observers concentrating entirely on rating without having to attend to the dynamics of the interview. In treatment trials the ratings can be made blind to time. The verbal component can be used for analysis of content and thought disorder. Above all, it is possible to make measurements, as opposed to ordinal ratings; for example, one can measure the latency of response (initial pause time), which Ahmed and Brockington (unpublished observations) have shown to have high test-retest reliability ($r = .9994$) and a high correlation with observer ratings of retardation ($r = .79$). Contrary to expectation, a videotaped interview is well tolerated by psychotic patients; in the Manchester study (Downing, Francis, and Brockington 1980), 48 of 50 patients had a 5- to 10-minute recorded interview shortly after admission. The disadvantages of the method are that a very brief sample of an episode can be recorded and only under artificial conditions; moreover, the analysis is extremely time-consuming.

Perhaps for this reason little work has so far been done on the use of the videotaped interview in clinical or nosological studies. Katz and Itil (1974) have shown that videotaped ratings were far more sensitive to changes produced by thioridazine and thiothixine in elderly patients than interview ratings using the Brief Psychiatric Rating Scales. One could envisage an expanded role for this investigatory tool. One or more 15- to 20-minute interviews during the most disturbed phase could be compared to a similar interview at the time of discharge. They would be focused on the patient's present concerns and recent events, providing material for an analysis of verbal content, measurements of speech, and ratings of affect. They would take over some of the functions of the structured psychiatric interview, which could then be used for a deeper exploration of particular areas. For example, it would be possible to devote more time to the analysis of delusions, not simply identifying the presence of ideas of grandeur or persecution, for example, but exploring their origin, structure, and extent. This might lead to the development of better measures of delusional thinking which would help in the differentiation of paranoid psychoses from other forms of schizophrenia.

An Illustrative Case. The following case illustrates how data from several sources contribute to the full picture of a psychotic episode:

> The patient was a 30-year-old woman repatriated from Africa, where she suddenly became disturbed while living in a small American enclave which a hostile government wanted to close down. When formally interviewed the day after admission, she was lethargic (heavily sedated) and replied evasively. She gave conflicting accounts of having excessive energy (e.g., gardening in the early morning) and diminished energy. She said she was being watched and whispered the words "Russians," "persecution," "airplanes and things," and "making noises and lights flashing and banging and everything." She had "not really wanted to carry on" and had wanted to "end everything so that nobody would have any problems." She was slightly disinhibited, making personal comments on the examiner's legs. The interview was considered severely impaired in quality, but ratings were made of denial of abnormality, self-neglect, nonsocial speech, drowsiness, suspiciousness, incongruous laughter, and loss of reserve.
>
> A second interview was held the following day. She was more open this time and admitted that she thought she was being "bugged" at the first interview. She described an extensive delusional system, believing that she was being watched, was going to be killed, and was a link in an international conspiracy. She had had visual misinterpretations, and gustatory and olfactory hallucinations. She had been extremely frightened and had acted on her delusional ideas. She had abused alcohol and had made an impulsive suicide attempt. Ratings of impaired concentration and errors on cognitive testing were made.
>
> Her husband was interviewed via a French interpreter. He said she had been depressed for some weeks before the onset of the acute disturbance, with anorexia and loss of weight. He described her overtalkativeness and her fear amounting to panic during the acute disturbance. He corroborated the account of her delusions but emphasized that they were largely consistent with the reality of life; for example, she had witnessed the sabotage of a car shortly before the onset of her illness.
>
> In the case folder was a narrative description written by a student nurse. She described the evolution of the delusional system, including the fact that the patient accused her husband of betraying her to the authorities. When she arrived in Britain she remained awake all night talking to herself and was physically aggressive to her family. She said she was a British secret agent. On admission she smiled secretively, seemed not to hear questions addressed to her, and replied monosyllabically. When introduced to the patients in her dormitory, she was immediately drawn to one of the same age and social standing and clung to her as a child to its mother. She wore a perplexed expression and allowed herself to be led by the hand, constantly asking simple questions like "Will you take me to the toilet?" She drew simple childish sketches of her house and family, at a 4-year-old level, annotating them with words like "unhappening" and "unreligious." In contrast to her normal personality, she was constantly going to the chapel, and wandered about in a scanty nightgown, heedless of the stares of the male patients. She behaved seductively. Her mood varied between fear, perplexity, and excitement when she would talk very quickly and giggle. All this behavior subsided completely within 2–3 days. She lost her delusions and said, "How can I have been so silly as to believe that my husband was against me!" After this rapid recovery she appeared to be a well-

adjusted, mature, and sensible woman.

None of the sources gave a full picture of this complex delusional psychosis (bouffée délirante), with its manic and paranoid elements. They each make a useful contribution. Although the student was untrained in psychiatry, her description is so clear and authentic that one has no hesitation in placing her evidence on the same level as the other data.

Ratings and the Need for Narrative. For statistical purposes, observations must be converted into numerical ratings at some stage. Commonly this is done on the spot, sometimes by junior investigators working alone. They may not record the reasons for their decisions, so that it is impossible to compare the basis for their judgments with other data. This practice stems from the belief that "instruments" like structured mental state examinations have an intrinsically high reliability. Too much emphasis has been attached to the higher interrater reliabilities—for example, coefficients of 0.73–0.77 for various editions of the Present State Examination (Wing et al. 1967; Kendell et al. 1968; World Health Organization 1973) obtained by senior co-trained researchers who knew that their reliability was being measured. This does not guarantee the reliability of ratings made under completely different conditions. It has been shown that reliability drops sharply as soon as observers believe they are no longer being monitored (Reid 1970; Taplin and Reid 1973). For this reason, it seems essential, at least in research on small samples, for all ratings to be made by two persons.

The practice of rating all information at source is also unsatisfactory because it results in too many ratings. As more and more rating scales are introduced, researchers come under pressure to complete many schedules in an effort to make their findings comparable with those of other centers. The same effect results from the use of multiple information sources. The number of ratings greatly exceeds the number of patients, and spurious correlations can readily be generated. It becomes necessary to condense the data by some form of algorithm (e.g., principal component analysis), which is surprisingly time-consuming. The combination of sophisticated mathematics with suspect data seems unwarranted.

An alternative method is to postpone ratings until the whole data base has been assembled. According to this policy, rating should be done only once, by a team of several raters, including the most senior investigators. The only material worthy of this effort is the whole body of information obtained from all sources. The raters review the patient's dossier at one sitting, working independently at first, knowing that they may have to defend their decisions to their colleagues. Master ratings (or consensus ratings) are obtained by computation or (with more expenditure of time) by resolving disagreements. The time taken (e.g., 40 minutes per rater per dossier, and more for discussion) is considerable, but the ratings which emerge are of superior quality. This method requires the use of narrative as the medium through which evidence is compared. The interview is used not as a source of ratings but as a source of information, and it is necessary to write down what is said at the rate of about 15 words/minute while conducting it. The descriptive powers of everyone in contact with the patient are at a premium, and (unless the data can be transcribed) legible handwriting is an asset.

The use of multiple information sources does not eliminate the problem of unreliability. It may even accentuate it. If there are many sources, there are more opportunities for conflict between reports, and the rater will have to exercise his judgment when deciding which to believe. Empirically it was found in the Manchester study that the interrater reliability of ratings made from a complete dossier was not high (Downing, Francis, and Brockington 1980). It reached a satisfactory level (Pearson's r at least .7, or Cohen's Kappa at least .5) in only 32 of 57 items and scales. For this reason it is essential to use at least two raters when making ratings in this way.

One can debate the relative merits of number and narrative as the proper mode for recording primary observations in this field of science. The advantages of narrative are, firstly, that critical faculties can be used to weigh up the evidence, comparing one statement with another. Without a written record one can only average the numbers, or accept judgments on authority. Secondly, language is far richer and more flexible than any system of ratings could become, and it allows the possibility of innovation, discovering new concepts of psychopathology or new diagnostic systems. Numerical ratings are already carved in stone. Narrative, especially if it avoids professional jargon and keeps close to events and statements, can be reinterpreted in terms of different systems of ideas. For example, the U.S./U.K. Diagnostic Project was concerned with Kraepelinian diagnosis, emphasizing characteristic symptoms like those of Schneider, and there was no intention to study other diagnostic ideas. Fortunately there was sufficient description in the schedules for Perris to make diagnoses of cycloid psychosis based on an entirely different set of pathognomonic symptoms, so that the data were used for a nosological study which was not envisaged in the original plan (Brockington et al. 1982). Once an episode has been documented in narrative form, it can be employed for diagnostic work anywhere, at any time, so long as that language is understood.

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A 15-Year Followup of 646 Schizophrenic Outpatients

by David M. Engelhardt, Bernard Rosen, Judith Feldman, Jo Ann Z. Engelhardt, and Patricia Cohen

Abstract

The 15-year hospitalization course of 646 chronic schizophrenic outpatients treated between 1958 and 1963 was determined using records of the research clinic, the Kings County Psychiatric Hospital, and the New York State Department of Mental Hygiene. The cohort was heterogeneous with regard to previous history of hospitalization: 20.6 percent had never been hospitalized, 22.0 percent had experienced only crisis admissions, and 57.4 percent had experienced long-term psychiatric hospitalization. The results indicate that 58.8 percent were hospitalized subsequent to project entry. A relationship was observed between previous history of hospitalization and hospitalization during the followup period. Patients with no previous history of hospitalization were less likely to be hospitalized than patients with crisis admissions only, who in turn were less likely to be hospitalized than patients with a history of hospitalization in a long-term psychiatric treatment facility (39.1 percent vs. 53.5 percent vs. 67.9 percent; $p < .001$). The implications of these findings for future followup studies are discussed.

This is the first of a series of reports on a 15-year followup of the hospitalization course of 646 schizophrenic outpatients who participated in a federally funded research project that began in 1958. The project, *A Study of Ataractics in Schizophrenic Outpatients* (U.S.P.H.S. MH–01983), was designed to establish the feasibility of maintaining schizophrenic patients in the community on a program of drug treatment and supportive psychotherapy. This project was one of the earliest attempts to evaluate, under double-blind, placebo-controlled conditions, the long-term effects of phenothiazine treatment in a group of schizophrenic outpatients (Engelhardt and Freedman 1961, 1969; Engelhardt et al. 1963, 1967; Cohen et al. 1968; Engelhardt and Margolis 1970).

This initial report will deal with the various parameters of the hospitalization course of these patients over a period of 15 years following their entry into the project. We were prompted to conduct a historical prospective study for a variety of reasons:

1. Our sample was composed exclusively of outpatients referred to our research clinic for maintenance pharmacotherapy. We thus had the unique opportunity of studying course of illness in a group of schizophrenic patients seeking outpatient treatment. Most studies examining the future hospitalization course of schizophrenic patients begin with already hospitalized patients, either upon admission or discharge.

2. Among our 646 schizophrenic outpatients, there was a significant proportion (21 percent) who had no history of psychiatric hospitalization before entering treatment at our clinic. From an epidemiological point of view, this group is of extreme importance since it contains patients who may never appear in a psychiatric hospital and, therefore, may not be represented

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in traditional hospital-based followup studies.

3. We were in a position to follow the hospitalization course of all of our patients over an extended period of time, a minimum of 14.5 years. We, therefore, avoided those problems so often besetting followup studies of patients who·

- Had been at risk for hospitalization for only relatively short periods of time, or
- Had been followed for varying lengths of time and, therefore, differed with respect to the period at risk for hospitalization.

4. The nature of our data permitted presentation of cumulative hospitalization rates separately for each followup year. Thus, it was felt that our data could reveal valuable information about the hospitalization course of schizophrenic patients not provided by classical, hospital-based followup studies.

Population and Procedures

The original project was carried out at the Psychopharmacology Treatment and Research Clinic of the Kings County Hospital Center in Brooklyn, New York. Between March 1958 and February 1962, 670 patients were admitted to the study. The majority of these patients (62 percent) were drawn from the intake of the Mental Health Clinic of the Kings County Hospital Center. A smaller number (12 percent) were discharged patients referred from the acute observation wards of the Kings County Psychiatric Service. The remaining 26 percent were referred by state hospital aftercare programs in the community.

To qualify for admission to the project, patients were required to be between the ages of 18 and 45, have a primary diagnosis of schizophrenia based on *DSM–II* criteria, and give evidence of mental illness of at least 1 year's duration. In fact, the patients admitted were generally chronically ill. More than half our sample showed signs of mental illness for 10 or more years before admission to the project. The patients displayed considerable variability in the amount and type of psychiatric treatment received before clinic admission. Eleven percent of the sample had never received any type of psychiatric treatment, 10 percent had received outpatient treatment only, and 30 percent had been hospitalized less than 90 days in aggregate before clinic admission. Twenty-five percent of our sample had an aggregate history of hospitalization in excess of 1 year.

Upon admission to the project, patients were randomly assigned to either placebo, chlorpromazine, or promazine treatment and were treated under double-blind conditions. Clinic visits were scheduled weekly for the first month, biweekly for the next 2 months, and monthly thereafter. Patients were free to leave the clinic at will with no attempt being made to pressure their return. When a clinic appointment was missed, a postcard with a new appointment was sent. If the patient failed to keep this appointment, he was dropped from the project. Average duration of clinic attendance was 20.6 months. However, the median length of stay was 5.6 months. Only 20 percent of the patients attended the research clinic for more than 2 years.

The patients were relatively young (mean age 30.4 years with a median of 30.7 years). Slightly more than half the sample (53.6 percent) were males. The patients were representative of the Borough of Brooklyn at the time of intake into this study. Sixty-eight percent were white, 28 percent were black, and 4 percent were Hispanic. Thirty-six percent were Protestant, 29 percent Catholic, and 35 percent Jewish. Three-quarters of the patients were in the lower two socioeconomic classes (IV, V) as measured by Hollingshead's Two Factor Index of Social Position. Forty-seven percent of our sample had not been married up to the time of admission to the clinic. Of the 53 percent who had been married, almost one third were separated, divorced, or widowed.

Slightly more than one third of the patients could be considered as functioning in "independent" roles, either as self-supporting or supported by a spouse. Forty-five percent were supported by relatives, usually parents, and 19 percent were recipients of public assistance. For those patients for whom employment was role appropriate (students and housewives were excluded) only 27 percent had a "good-to-excellent" history of employment, suggesting fairly regular employment; 21 percent had a "fair-to-poor" work history with sporadic employment; and 52 percent had rarely or never been employed. The employment history of our sample of outpatient schizophrenics was thus very similar to that reported in the literature for ambulatory schizophrenic patients in general (Mosher et al. 1971; Anthony et al. 1972).

This observed variability in functioning level, as well as in previous psychiatric treatment history, is consistent with the view of many experts that schizophrenia is not a unitary disorder, but comprises a number of subgroups which differ significantly with respect to clinical course and outcome. The followup data to be presented in this study further confirm the notion of heterogeneity among schizophrenic patients with respect to clinical course.

Followup data were gathered through December 31, 1977, providing for a possible followup period ranging from 15 to 20 years depending on date of admission to the project. To allow for a uniform followup period for each patient, the actual end of the followup period ranged from December 31, 1972, for patients admitted in 1958, to December 31, 1977, for patients admitted during 1963. Because patients were admitted to the study in relatively equal numbers during each month of a project entry year, the postproject-entry followup time for the group as a whole averaged 6 months during the first year of the followup with an additional 12 months added during each succeeding year for an average followup of roughly 14½ years.

Although some project patients continued to return to the clinic from time to time, permitting a "real live" followup, the major source of hospitalization data for patients, subsequent to leaving the project, was the records of the New York State Department of Mental Hygiene, and the Kings County Psychiatric Hospital.

For each of the 670 patients admitted to the outpatient project, we provided the statistical division of the New York State Department of Mental Hygiene the full name and last known address, as well as additional identifying data such as birth date, maiden name, and name of spouse and other relatives to assure accurate identification. The Department then returned to us, for each patient with a record of hospitalization, the dates of admission and discharge for each hospitalization (both public and voluntary) in chronological order from the patient's first recorded hospitalization through December 31, 1977.

Independent checks using data on hospitalization in our clinic files, as well as from the Kings County Hospital Center Record Room, satisfied us that the Department of Mental Hygiene's search was comprehensive and thorough. The admission and discharge records of the Kings County Psychiatric Hospital were valuable, not only as a check on the Department of Mental Hygiene's records, but also as a source of information regarding those crisis admissions which resulted in return to the community as opposed to transfer to a long-term psychiatric treatment facility.

Information with regard to diagnosis was also obtained from the New York State Department of Mental Hygiene and the Kings County Psychiatric Hospital for the 565 patients in our sample (87.5 percent) who had been hospitalized either before or after admission to the original project. On the basis of this information we were able to verify the diagnosis of schizophrenia in 97 percent of the patients who had been hospitalized at least once.

A word of caution is in order regarding the limitations of the postclinic data. Data on crisis admissions in Boroughs of New York City other than Brooklyn were basically not available to us (except in those few instances when we received a request for information from the admitting hospital). The probable data loss here is minimal if preclinic data on out-of-borough crisis admissions can be used as a guide. Only 3 percent of the crisis admissions during the preclinic period occurred at out-of-borough municipal hospitals. Our preclinic data were derived from lengthy detailed interviews with the patients and a close relative which were then cross-checked against existing hospital records and found to be better than 98 percent accurate.

Some loss of hospitalization data could stem from the possibility that some of our male patients who had served in the military were admitted directly to federal hospitals without appearing in the Department of Mental Hygiene or the Kings County Psychiatric Hospital's records. With respect to veterans passing through Kings County Hospital, they generally were transferred to state rather than federal hospitals because of the shortage of beds at local VA facilities. For these patients, discharge from the state hospital generally occurred before the availability of a VA bed. The Kings County Record Room data indicate that only one veteran in our group was transferred directly to a VA hospital from the Kings County Psychiatric Hospital. With regard to the state data, no veteran in our group was transferred from a state hospital to a VA hospital.

For those of our patients who may have left New York State between the time of departure from the research clinic and December 31, 1977, and who may have been hospitalized out of state, we must assume their existence without any clear idea of the numbers involved. A rough estimate of the magnitude of this problem can be obtained from the fact that only three requests for clinical summaries were received from out-of-state treatment services through December 31, 1977. However, the possibility exists that the data to be presented with respect to hospitalization may tend to underestimate the actual incidence and occurrence of hospitalization.

As of December 31, 1977, we were able to identify 24 patients, out of the original group of 670, who had died during the followup period. These patients have been excluded from presentation in order to provide uniform data on all patients for each year of the followup period. Thus, we will report on the hospitalization course of 646 patients.

Results

First we will consider the cumulative hospitalization rates for the full cohort of 646 patients. As can be seen in the first row of table 1, 58.8 percent of our cohort had been hospitalized at least once during the 15-year followup period. It is of interest that of the 646 patients, 266, or 41.2 percent, escaped hospitalization during the 15 years of followup.

The cumulative incidence of hospitalization reported in this study (table 1) is similar to that reported in the literature for heterogeneous groups of previously hospitalized patients. The rates reported in the literature range between 23 and 42 percent at 1 year (Sanders, Smith, and Weinman 1967; Silverstein 1968; Bockoven and Solomon 1975; Gove and Fain 1977); between 38 and 57 percent at 2 years (Orlinsky and D'Elia 1964; Hargreaves et al. 1977; Leaf 1977; Matthews et al. 1979; Watt and Szulecka 1979); and between 30 and 60 percent at 3 years (Sanders, Smith, and Weinman 1967; Silverstein 1968; Bockoven and Solomon 1975; Mattes, Rosen, and Klein 1977). Bland and Parker (1976) report that at an average of 11.5 years (range of 10–12 years) after discharge, only 63.6 percent of first admissions were rehospitalized. Ciompi (1980) reported that only 53 percent of his cohort had been rehospitalized during the average of 37 years following release from their first hospitalization.

The second row of table 1 presents cumulative hospitalization rates only for the 380 patients who were hospitalized. As can be seen, roughly two thirds (63 percent) of those patients destined to be hospitalized were hospitalized by the end of the second followup year. By the end of the fifth followup year, 84.7 percent of these patients had been hospitalized at least once, and by the end of the seventh year after clinic admission over 90 percent had been hospitalized.

The number of hospitalizations for the 380 hospitalized patients ranged from 1 (*n* = 148, or 39 percent) to 15 (*n* = 1) with an average

Table 1. Cumulative percent hospitalized by postadmission followup year

	Postadmission followup year														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Cumulative % hospitalized (*n* = 646)	22.3	37.2	42.1	45.7	49.8	51.7	53.6	54.5	56.0	56.7	57.4	57.7	58.0	58.5	58.8
Cumulative % hospitalized of those eventually hospitalized (*n* = 380)	37.9	63.3	71.5	77.7	84.7	87.9	91.2	92.7	95.2	96.4	97.6	98.1	98.6	99.5	100.0

of 2.7 and a median of 2. This compares favorably with the median of 2 and the average of 3.14 hospitalizations reported by Bland and Parker (1976) for the 56 patients who had been rehospitalized in their study.

The average length of a single hospitalization was 16.4 months for the 380 patients who were hospitalized. However, there were some patients whose solitary hospitalization exceeded 6 years, while a number of patients who had experienced three or more hospitalizations during the followup period accumulated less than 1 year's aggregate time in a hospital.

The patients in our study were hospitalized an average of 44.4 months with a median of 28.9 months and a range of from 1 to 174 months. About 20 percent spent an aggregate of less than 3 months in mental institutions, while another 20 percent of those hospitalized accumulated over 7 years (about half of the followup period) in psychiatric hospitals. The 76 patients who had been hospitalized more than 7 years represent 11.8 percent of our entire group of 646 patients. This is similar to the findings of Huber et al. (1980) who followed up, for an average of 22.4 years, a group of patients first hospitalized between 1945 and 1959. Of these patients 13.3 percent were permanently hospitalized. Similarly Ciompi (1980) found that after an average followup period of 37 years, 14 percent of the patients had spent 80 percent or more of the followup period in a psychiatric hospital.

We now turn from a description of the cumulative hospitalization experience of our cohort to a description of yearly hospital utilization patterns as presented in table 2.

The first part of table 2 presents the proportion of the entire group (n = 646) who were in the hospital at least 1 day during each followup year. As can be seen, the proportion of patients using psychiatric hospital facilities during any 1 year ranged from a high of 34.7 percent in year 2, to 11.6 percent in the last year of the followup. Beginning with year 3, there is a steady decline in the proportion of patients spending at least 1 day in a psychiatric hospital, leveling off below 13 percent beginning with year 12.

In view of the uncertainty as to the fate of those patients for whom no record of hospitalization was found, the possibility must be considered that the decreasing risk for hospitalization may have been a function of sample attrition, that is, patients leaving New York State and thus lost to followup. However, it is our impression that this is not the case. The similarity of our findings with other short- and long-term followup studies previously cited suggests that the pattern of our results supports the contention of Bleuler (1968, 1972), Huber et al. (1980), and Ciompi (1980) that schizophrenia does not seem to be a disease of slow progressive deterioration. As Vaillant (1978) points out:

> Bleuler has been able to arrive at the novel conclusion that it is only for the first 5 years that Kraepelinian deterioration may occur. Then, if even modest

Table 2. Proportion of patients residing in a psychiatric hospital, mean number of admissions, and mean number of months hospitalized during each followup year

Postadmission followup year														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
A. Proportion of patients residing in a psychiatric hospital (n = 646)														
21.7	34.7	32.4	31.1	30.3	28.3	26.5	22.4	20.6	17.3	15.2	12.7	12.5	12.5	11.6
B. Mean number of admissions (hospitalized patients only; n = 380)														
0.41	0.33	0.15	0.19	0.19	0.17	0.16	0.15	0.18	0.12	0.14	0.10	0.12	0.15	0.15
C. Mean number of months hospitalized (hospitalized patients only; n = 380)														
1.56	4.73	5.01	4.58	4.37	4.15	3.77	3.30	2.93	2.42	1.97	1.75	1.39	1.24	1.32

> rehabilitative efforts are sustained, a clinical plateau or even gradual improvement occurs in the most chronic cases. [p. 21]

The second row of table 2 presents the mean number of admissions to a psychiatric facility, for each year of the followup period, for the 380 patients who were hospitalized. As can be seen in the table, the mean number of admissions during the first and second years (0.41 and 0.33) is relatively high. After the second year the mean number of admissions drops by more than half to 0.15 and fluctuates thereafter between 0.10 and 0.19 admissions per year with an average of 0.15 admissions for each of the remaining 13 years.

The third row of table 2 presents data with regard to the mean number of months of hospitalization in each followup year for the 380 patients who were hospitalized. As can be seen, the mean number of months the patients spent in the hospital each year reaches a peak of 5.01 months in the third followup year and declines consistently thereafter.

During our followup period, spanning the calendar years of 1958 to 1977, dramatic changes were taking place in psychiatric hospitals throughout the country. The number of patients in mental hospitals, which had exceeded half a million in 1950, had declined steadily to a current low of about 170,000 patients.

An energetic policy of deinstitutionalization led to a marked shortening of hospital stay, which now averages, nationally, less than 4 weeks. At the same time there has been a marked increase in readmission rates. In 1950 about 25 percent of admissions to state hospitals represented previously hospitalized patients. By 1972 the percentage had risen to 64 percent (Ozarin, Redick, and Taube 1976). This high rate of readmissions has been referred to as the "revolving door" phenomenon.

If we reexamine the data presented in table 2, there is little to suggest a "revolving door." We find in our group of patients a progressive decline in the proportion of patients using psychiatric hospital facilities, and a leveling off of the mean number of admissions to psychiatric hospitals as we follow our cohort over 15 years. With respect to the mean number of months hospitalized, however, the marked decline observed is in full accord with the progressive trend toward shorter hospitalizations.

The hospitalization data presented thus far have dealt with the cohort of patients as if they constituted a homogeneous group, ignoring the likelihood of differences in propensity for hospitalization among subgroups of schizophrenic patients. The followup literature involving discharged schizophrenic patients makes reference to a number of predictors of posthospital course. Previous history of hospitalization has consistently emerged as a powerful predictor of future hospitalization (Buell and Anthony 1973; Rosenblatt and Mayer 1974).

To determine the relationship between previous history of psychiatric hospitalization and hospitalization course during the followup period, we divided the 646 patients in our cohort into three groups based on their hospitalization experience before entering the project (see table 3).

Group A consists of 133 patients (21 percent of the cohort) who had no previous history of psychiatric hospitalization before seeking treatment at our clinic. This is a group of patients who are totally unrepresented in classical followup studies.

Group B consists of 142 patients (22 percent of the cohort) who had experienced exclusively "crisis admissions" in a municipal hospital before project entry. Crisis admission is defined as a brief hospital stay, usually in a general hospital psychiatric reception service, with invariable return to the community. This group of patients is also highly unrepresented in classical followup studies.

Group C comprises the remaining 371 patients (57 percent of the cohort) whose preproject history included at least one admission to a long-term psychiatric treatment facility. This is the group generally reported on in followup studies.

We based our decision to segregate "crisis admissions" from hospitalizations in long-term psychiatric treatment facilities on several factors. Admission to a long-term treatment facility, as opposed to a crisis admission, generally involves a prolonged period of hospitalization and major disruption of the patient's life. Furthermore, admission to a long-term psychiatric facility often stigmatizes the patient for the rest of his life in the eyes, not only of family members, but of mental health professionals as well, resulting in diminished acceptance by the community and increased likelihood of rehospitalization.

Table 3 presents the cumulative incidence of hospitalization over the 15 years of followup for each of the three hospitalization history groups defined above. As can be

Table 3. Cumulative percent hospitalized by preadmission hospitalization history group and postadmission followup year (n = 646)

Preadmission hospitalization history groups[1]	Postadmission followup year														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
A. Never hospitalized (n = 133)	15.0	23.3	27.1	28.6	33.1	35.3	36.8	36.8	38.3	38.3	39.1	39.1	39.1	39.1	39.1
B. Crisis admission only (n = 142)	16.9	31.7	38.7	41.5	46.5	48.6	48.6	50.7	51.4	52.8	52.8	52.8	52.8	53.5	53.5
C. Long-term treatment facility (n = 371)	27.0	44.2	48.8	53.4	57.4	59.6	61.5	63.1	64.4	65.2	65.8	66.3	66.8	67.4	67.9

[1] Differences across all three groups are significant for all years ($p < .001$); differences between groups A and B are significant ($p < .05$) for all but years 1 and 2; differences between groups B and C are significant for all years ($p < .05$).

seen in table 3, there is a continuous ordinal relationship between previous history of hospitalization and incidence of hospitalization for each year of the followup period. By year 15, 39.1 percent of the patients with no previous history of hospitalization were hospitalized as compared to 53.5 percent of those with a history of only crisis admissions, and 67.9 percent of those with previous long-term hospitalization.

It is of interest to note that the 12-year cumulative hospitalization rate of 62.6 percent for our previously hospitalized patients (groups B and C) was almost identical with the 63.6 percent reported by Bland and Parker (1976) after an average of 11.5 years of followup.

Statistical analysis (chi square) revealed that the incidence of hospitalization of the three groups differed significantly for each of the followup years ($p < .001$). For each year the groups maintained their ordinal position, with group A having the lowest and group C having the highest cumulative incidence of hospitalization. The crisis admission group, group B, occupied the middle position. Thus our data are consistent with general findings that previous performance predicts future performance with respect to incidence of hospitalization, even when prediction is made at the point of entry to an outpatient treatment setting, rather than at the point of hospital discharge.

Previous history of hospitalization also significantly predicted duration and number of hospitalizations during the followup period for the entire group of 646 patients ($p < .001$). The mean duration of hospitalization over the 15-year followup period was 15.44 months for group A, 15.17 months for group B, and 34.61 months for group C. The mean number of hospitalizations was 1.03 for group A, 1.16 for group B, and 1.96 for group C.

This pattern of results justifies our decision to separate out the crisis admission group (group B) from the group of hospitalized patients. As the data indicate, the proportion of patients hospitalized in group B (53.5 percent) was significantly less than the proportion hospitalized in group C (67.9 percent; $p < .05$). With respect to group A, the proportion of patients hospitalized (39.1 percent) was significantly less than the proportion hospitalized in group B (53.5 percent; $p < .02$). However, with respect to mean duration and number of hospitalizations, groups A and B were statistically similar to each other and both significantly lower than group C ($p < .01$).

Table 4 presents cumulative hospitalization rates only for the 380 patients actually hospitalized. The cumulative hospitalization rate is almost identical for the three groups in each year of the followup period.

While history of previous hospitalization seems to have a powerful influence on whether a patient becomes hospitalized, this factor appears to have no effect on the rapidity with which hospitalization occurs, when it does occur, postclinic admission.

Previous history of hospitalization is clearly a powerful factor influencing a patient's potential for rehospitalization. However, it is important to recognize that it does not have a universal, overriding effect. Table 5 highlights the limitations of previous history of hospitalization as a predictor of future hospitalization.

On an overall basis, table 5 indicates that 41.2 percent of the cohort of 646 patients had succeeded in maintaining community status, free of any type of psychiatric hospitalization, with an additional 44 patients (6.8 percent) experiencing only crisis admissions during the followup period. Thus 48 percent, almost half of the original group of patients who entered the project, had successfully escaped major psychiatric hospitalization during the 15-year followup period.

Of particular interest are the 141 patients in group C (119 not hospitalized and 22 with only a crisis admission) who experienced no major psychiatric hospitalization postproject entry despite a history of previous admissions to long-term psychiatric treatment facilities. These 141 patients had been hospitalized on the average 29 months before entering the research project. This can by no means be viewed as an insignificant period of previous hospitalization.

Table 4. Cumulative percent hospitalized by preadmission hospitalization history group and postadmission followup year for hospitalized patients only (n = 380)

	Postadmission followup year														
Preadmission hospitalization history group	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Never hospitalized (n = 52)	38.5	59.6	69.2	73.1	84.6	90.4	94.2	94.2	98.1	98.1	100.0	.....	.....	.....	.....
Crisis admission only (n = 76)	31.6	59.2	72.4	77.6	85.5	86.8	90.8	90.8	94.7	96.0	98.7	98.7	98.7	100.0	.....
Long-term treatment facility (n = 252)	39.7	65.1	71.8	78.6	84.5	87.7	90.5	92.8	94.8	96.0	96.8	97.6	98.4	99.2	100.0

Table 5. Type of postadmission hospitalization experience by preadmission hospitalization history group

Preadmission hospitalization history group	Type of postadmission hospitalization experience					
	None		Crisis only		Long-term	
	n	%	*n*	%	*n*	%
A. Never (*n* = 133)	81	60.9	6	4.5	46	34.6
B. Crisis only (*n* = 142)	66	46.5	16	11.3	60	42.2
C. Long Term (*n* = 371)	119	32.1	22	5.9	230	62.0
Total group (*n* = 646)	266	41.2	44	6.8	336	52.0

While 52 percent of the 646 patients experienced major psychiatric hospitalizations at some time during the followup period, for 48 percent the clinical course was characterized basically by a community mode of adjustment to their illnesses. This picture of the clinical course of the chronic schizophrenic patient is considerably at odds with the view, originally presented by Kraepelin (1919), that schizophrenia is a progressive nonremitting illness with an inevitable deteriorating prognosis leading to the expectation that most chronic schizophrenics are destined, sooner or later, to become hospitalized, and once hospitalized to experience recurrent hospitalizations. One possible explanation for this is that as many as 25–50 percent of schizophrenic patients are not represented in classical followup studies which are limited to patients already admitted to or discharged from a long-term treatment facility.

Table 5 further indicates that of the 646 patients, 81, or 12.5 percent, had completely escaped hospitalization during their lifetimes. An additional 88 patients (13.6 percent) had experienced only crisis admissions. In other words, we could find no evidence of a major psychiatric hospitalization for over one-quarter (26.2 percent) of the 646 schizophrenic patients. It is notable in this context that the mean age of the cohort at the conclusion of the followup period was 45 years with an age range of 33 to 60.

Discussion

The results of our 15-year followup, involving 646 schizophrenic outpatients admitted to a community clinic, are consistent with the findings of other long-term followup studies (Bleuler 1968, 1972; Bland and Parker 1976; Stephens 1978; Ciompi 1980; Huber et al. 1980) which showed a relatively favorable long-term course for schizophrenic patients. These results also support previous findings (Buell and Anthony 1973; Rosenblatt and Mayer 1974) with regard to a significant relationship between previous and subsequent hospitalization course. However, it is of considerable import that among our most *hospitalization prone* patients, fully 38 percent experienced no major psychiatric hospitalization over the course of 15 years.

Assuming that our group of 646 patients is representative of the chronic schizophrenic population at large, then the results of our 15-year followup study raise some serious questions about current approaches for the provision of services to the chronically ill schizophrenic patient. The shift in the last decade from the hospital to the community as the setting of choice for maintenance treatment, while laudatory in many ways, fails to provide for the specific needs of a sizable number of schizophrenic patients.

While there is a large group of schizophrenic patients, 48 percent in our cohort, who probably make little or no use of inpatient psychiatric treatment facilities during their lifetimes, and who would, no doubt, be best served by long-term outpatient treatment, 52 percent of chronic schizophrenic patients will need repeated and at times prolonged access to inpatient facilities. For the most vulnerable group, the 371 patients who had experienced at least one admission to a long-term psychiatric treatment facility before project entry, the probability of readmission to a psychiatric treatment facility during the followup period was almost 68 percent with a mean duration of hospitalization of 34.6 months.

In studying long-term prognosis, as it relates to the hospitalization of schizophrenic patients, one must start with a cohort of patients, ideally at the point the illness becomes manifest, and at least before a hospitalization has occurred. This is best exemplified by our group of 133 patients who had not been hospitalized before our followup study began. After 15 years of followup, 60.9 percent had remained in the community continuously. Thus, less than half of the individuals carrying a diagnosis of schizophrenia are likely to be represented in "classical" followup studies originating in-hospital. It is only by studying schizophrenic patients who have not yet experienced hospitalization that one can obtain the maximum heterogeneity possible in order to develop adequate data to understand the course and prognosis of schizophrenia.

There is a need for additional long-term studies starting at the point the schizophrenic patient first seeks psychiatric care. The community mental health center carries the primary responsibility for the pursuit of such followup studies.

A second need, if we are further to advance our knowledge of schizophrenia, is the intensive study of groups of patients whose clinical course does not follow expected patterns. Specifically, if we can understand why a substantial group of patients with a history of prefollowup hospitalization averaging 29 months were able to remain out of the hospital for the next 15 years, we may be able to improve our treatment methods and reduce the need for psychiatric hospitalization.

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Patient and Family Attitudes About Schizophrenia: Implications for Genetic Counseling

by Patricia M. Schulz, S. Charles Schulz, Eleanor Dibble, Steven D. Targum, Daniel P. van Kammen, and Elliot S. Gershon

Abstract

Psychiatrists are giving increased attention to genetic counseling for mental illness. However, the burden of these illnesses as perceived by families and the degree to which families feel a need for genetic counseling have yet to be established. Attitudes and perceptions measured in this study focus on etiology, familial risk, and socioeconomic burden of schizophrenia, as well as childbearing plans and the acceptability of genetic counseling. Members of 17 families, each with a child diagnosed schizophrenic, were studied using the Family Attitudes Questionnaire. The results demonstrate that the well family members view schizophrenia as a severe and debilitating illness. The results also show that there is a disparity between the attitudes of well family members and patients: 92 percent of parents compared to 25 percent of patients identified schizophrenia as a disorder associated with extreme burden. Regarding childbearing decisions, 29 percent of parents compared to 66 percent of patients say they would have children (in hindsight or in future) based on what they now know about schizophrenia in their family. This result corroborates reports from genetic counselors for other illnesses: the wish for children appears to override considerations of risk and burden for those potentially genetically affected persons who have not reached their desired family size.

Numerous studies have found that the incidence of schizophrenia is increased with biological relatedness (Rosenthal 1970; Kety 1971; Gottesman and Shields 1976; Kay 1978). Investigations have included exploratory studies and studies in which genes and environment were examined separately. Although the specific mechanisms of the transmission of schizophrenia have not been elucidated, several investigators have encouraged the use of genetic counseling in the comprehensive care of schizophrenic patients and their families (Reed 1972). Data about the attitudes of schizophrenic patients and their families concerning the illness are sparse in the literature.

Dimensions of the thinking of counselees, as they make a decision to have children or not when there is a risk of genetic illness, are not thoroughly understood (Murphy 1973). Common sense tells us that the decision process of schizophrenic patients would be more difficult for investigators to understand. Exploratory study is required to know more about the attitudes and information available to the potential counselee for psychiatric illnesses with a genetic component. Ordinarily, counsel ees are thought to consider the risk and the burden of an illness simultaneously. Genetic counselors give risk figures and a sense of the burden to consider regarding future offspring. Psychiatrists who give genetic counseling can provide schizophrenic patients and their families with risk figures arrived at through years of empirical studies. Similar data do not exist, however, for the impact of the burden of schizophrenia on the

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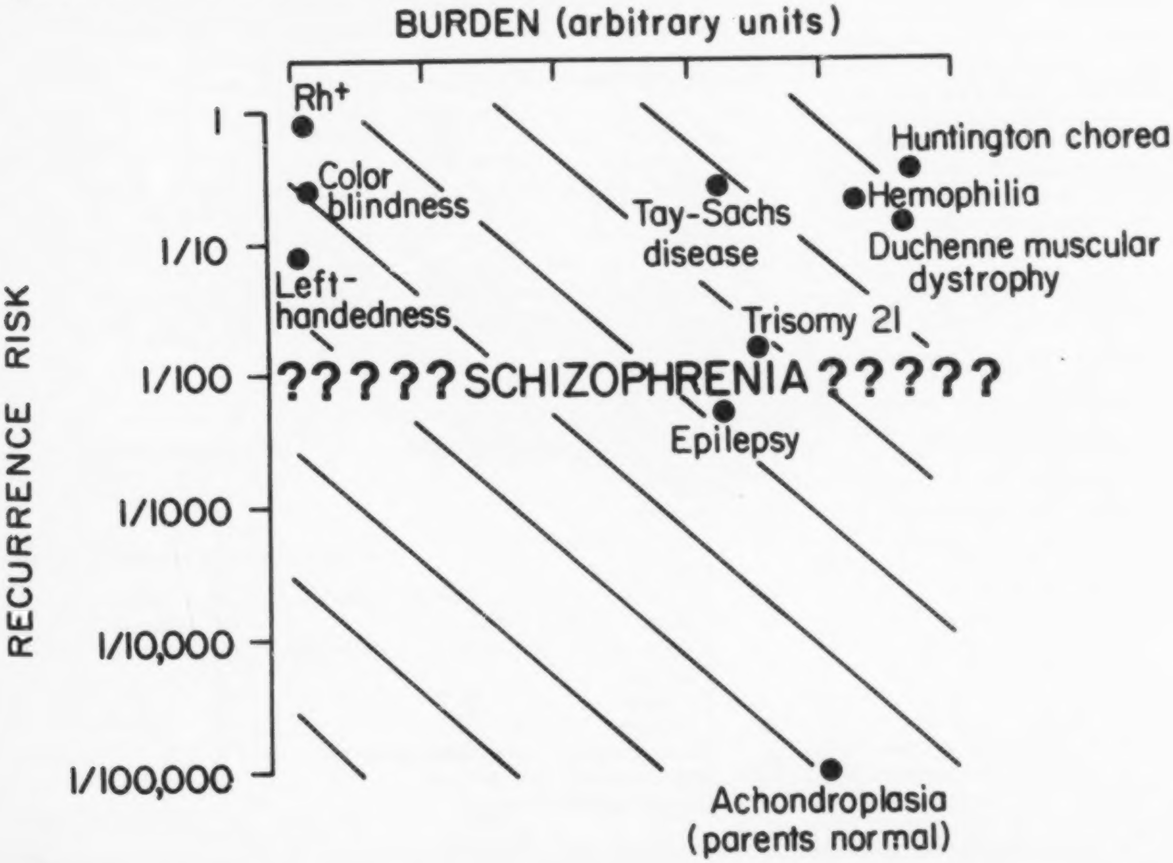
individual or his family, although this subject has been studied (Hoenig and Hamilton 1966; Sakamoto 1969; Kreisman and Joy 1974). There are few guidelines to share when counselees ask the psychiatric genetic counselor: (1) what is the risk of the illness? or (2) what do other families say is the burden of the illness? Tsuang (1978) has addressed this issue and has recommended systematic investigation of these questions.

The risk of schizophrenia, which varies depending on the psychiatric diagnosis of parents and other relatives, is well known (Erlenmeyer-Kimling 1976; Kessler 1980). The burden of schizophrenia on the family or their view of the illness has not been well quantified. The purpose of this investigation was to begin to quantitate the burden of schizophrenia to help future counselees perceive the risk-burden ratio on a graph such as the one made by Murphy for other genetic illnesses (figure 1). In addition, we present a sampling of attitudes toward genetic counseling.

Methods

This study was performed on a 12-bed schizophrenia inpatient unit at the Clinical Center of the National Institute of Mental Health (NIMH) in Bethesda, Maryland. Admissions to the NIMH Neuropsychopharmacology Section are not restricted to a defined

Figure 1. General dimensions of consultees' thinking



Adapted from Murphy (1973).

catchment area, and all patients must be referred by their psychiatrist. The average length of stay on the unit is 6–8 months. Patients participate in biological research and participate in a standard psychiatric milieu. Treatment is offered free of charge.

Shortly after admission to the unit, patients and their families were interviewed individually by one of the authors (PMS). Before being asked for information on the questionnaire, they were told that the study would explore their attitudes toward schizophrenia and childbearing, vis-à-vis their experience with the illness. All index probands had been diagnosed schizophrenic according to Research Diagnostic Criteria (RDC; Spitzer, Endicott, and Robins 1978). They were consecutive admissions from May 1979 to January 1980. Partial family units were included.

Tables 1 and 2 show the demographic characteristics of the probands and the socioeconomic standing of the families, respectively. Most of the families were in high income occupations. The total sample included 12 patients, 24 parents, and 8 siblings (table 3). All but four parents were married at the time of this study. Families began family therapy with the unit social worker shortly after admission, with the type of therapy depending on the needs of the individual family and with the underlying assumption that family conflicts would be addressed.

The Family Attitudes Questionnaire (FAQ) is a recently designed research measure with fixed alternative quantitative responses (Targum et al. 1981). The questionnaire was first used in a survey of bipolar patients and their families. We used the scale without modification because schizophrenia was part of its intended scope. Chi square and Fisher's exact tests were used to tabulate frequencies of response and to assess differences between family members.

Results

The first section of the FAQ explores the respondent's thoughts about the etiology and nature of schizophrenia. Four options were offered as possible causes of schizophrenia: biochemistry, heredity, interpersonal relations, and other causes (such as the environment, virus, or stress) (table 4). Eighty-seven percent of the parents identified biochemical abnormalities as the etiology of schizophrenia and, similarly, 75 percent of the patients and the well offspring responded that biochemical abnormalities cause schizophrenia. The patients identified a hereditary component 66 percent of the time, somewhat more often than their siblings and parents did (50 percent). The most disagreement about etiology between family members concerned the role of interpersonal relationships. Only 21 percent of the parents said that interpersonal relationships were causal compared to

Table 1. Proband Demography

Subject	Age (years)	Religion	Years ill	Diagnostic subtype	Prognostic score[1]
1	21	Protestant	2	Residual	7
2	22	Catholic	6	Chronic undifferentiated	3
3	24	Catholic	3	Hebephrenic	2
4	23	Catholic	15	Schizoaffective, mainly schizophrenic	8
5	31	Jewish	10	Chronic undifferentiated	Not obtained
6	28	Jewish	7	Chronic undifferentiated	Not obtained
7	26	Unaffiliated	8	Paranoid	8
8	19	Catholic	3	Paranoid	12
9	30	Jewish	2	Paranoid	2
10	23	Protestant	6	Schizoaffective, mainly schizophrenic	3
11	22	Protestant	4	Chronic undifferentiated	Not obtained
12	30	Protestant	4	Chronic undifferentiated	5

[1] Score is based on the modified prognostic scale of Strauss and Carpenter. The scale is scored 0–16, with a higher score indicating better premorbid adjustment.

Table 2. Highest occupational level obtained by head of family

Occupational level	*n*
Higher executive, proprietor of large concern, major professional	2
Business manager of large concern, proprietor of medium-sized business, lesser professional	6
Administrative personnel, owner of small independent business, minor professional, farmer	4
Clerical or sales worker, technician, owner of a little business, farmer	4
Skilled manual employee, farmer	
Machine operator, semiskilled employee, farmer	
Unskilled employee, farmer	
Parent never worked in paid employment	1
Total	17

50 percent of the patients and 75 percent of the siblings.

The sample's perception of the prevalence of schizophrenia in the general population was relatively accurate, with mothers and patients being inaccurate most often. When the siblings and patients were asked what the risk to their offspring would be, the siblings consistently overestimated the morbidity risk while 58 percent of the patients underestimated it (figure 2). Patients' estimates for dual matings were not assessed.

Table 3. Sample characteristics

Sample	Number	Sex	Age (years)
Patients	12	6 Male 6 Female	20–32
Parents	24	10 Male 14 Female	44–82
Siblings	8	3 Male 5 Female	16–37

The burden of the illness of schizophrenia on the family was the next topic explored. Respondents were asked to assess burden in a social and economic sense and not in terms of anguish or misery. The section evaluating burden was divided into two parts: acute and chronic. In the section on acute schizophrenia, the family members were asked to check the three most troubling characteristics of acute schizophrenia (figure 3).

The responses suggest that the positive symptoms of the illness, such as hallucinations, cause the worst social difficulties for the patients, while the negative symptoms, such as being unable to function, troubled one half of the patient sample. Hallucinating behavior was checked by half of the parents regarding the acute stages of schizophrenia, whereas the so-called negative symptoms of inability to function were identified by 87 percent of parents. The siblings of the patients associate social burden with increased suicidality, hallucinating behavior, and inability to function during the acute stage of the illness. The parents and siblings found their attitudes about acute episodes of the illness difficult to reconcile with the socioeconomic categories presented. Thirty percent of the respondents insisted on using the "other" category, with parents indicating personal and psychological burden as the most overwhelming. One parent said, "The worst part of the acute episodes is that he can't empathize with our grief, he can't tell that we care." Three parents had extreme statements for this "other" category. These parents' responses included "I wish for policy of euthanasia for persons such as those with schizophrenia," and "Nothing can be done for someone with schizophrenia except risky experimental treatments, I don't care how risky it is, I'd rather she were dead, really," and "I wish I could free my child from a deteriorating life's course that promises neither cure nor death."

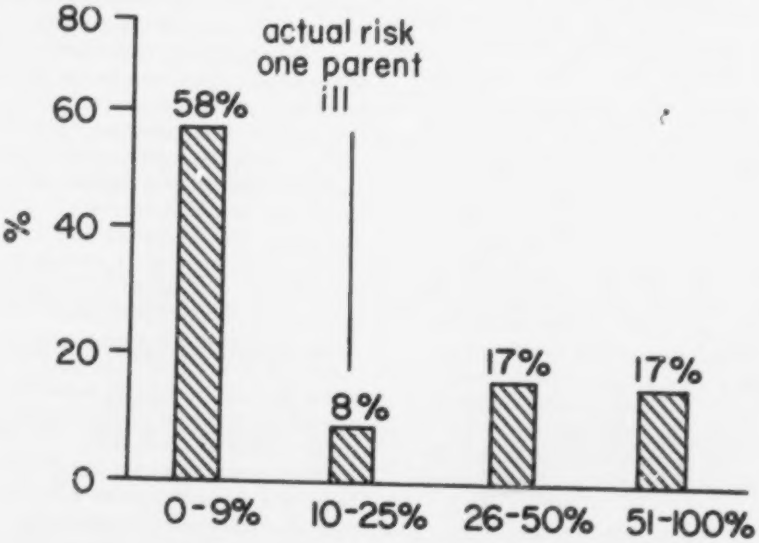
The respondents were then asked to check problems they felt to be associated with chronic schizophrenia (table 5). The patients invariably ranked fears of recurrence, frequent hospitaliza-

Table 4. Perception of etiology of schizophrenia[1]

Etiology	Patients ($n = 12$)	Siblings ($n = 8$)	Parents ($n = 24$)
Biochemical	75	75	87
Hereditary	66	50	50
Interpersonal	50	75	21
Other (e.g., injuries, stress, virus)	33	13	21

[1] Multiple responses permitted.

Figure 2. Estimated risk to children for schizophrenia by proband



tion, and financial strain as problems during the chronic stage of the illness. The parents most often identified fewer jobs, dependence on others, and financial strain as chronic problems associated with schizophrenia. The siblings identified fewer jobs, fears of recurrence, and trouble with the law. Table 5 reveals a general correlation of the views of all family members about the types of chronic burden.

In another question about chronic burden, 100 percent of the well family members saw schizophrenia as a disorder that could ruin the patient's life. Only 41 percent of the patients thought this was so. This difference was statistically significant ($p < .001$). Sixty-eight percent of all respondents identified schizophrenia as a long-term disabling illness as opposed to 16 percent who saw it as a short-term life crisis. One should remember that the probands in this group had been ill for an average period longer than 4 years.

To explore further the burden of schizophrenia on a family, the respondents were asked to rate separately the amount of family burden imposed by major medical and psychiatric illnesses. The patients saw cancer as the illness causing the most burden, but 8 of 12 also noted that schizophrenia causes a high or extreme burden (table 6). Interestingly the patients did recognize schizophrenia as a burden on the family. This result contrasts with that for the bipolar patients studied by Targum et al. (1981) who were much less aware of the burden of their psychiatric illness on the family. For the well family members, schizophrenia was perceived as causing the most burden (table 7). As one father put it, "I've known people who were cured of cancer, of all these illnesses, but I know of no one who was cured of schizophrenia."

The next portion of the FAQ dealt with views on childbearing. When asked if people with schizophrenia should have children, 75 percent of the patients said "yes," while 38 percent of the parents answered "yes they should." This difference is statistically significant ($p < .03$). There was no difference beteen the generations when respondents were asked the same question about people with mania and depression.

All of the parents in this study had completed their desired family size at the time of the study. They were asked if they would have had children if they "had it to do over

Figure 3. Most troubling characteristics of acute schizophrenia

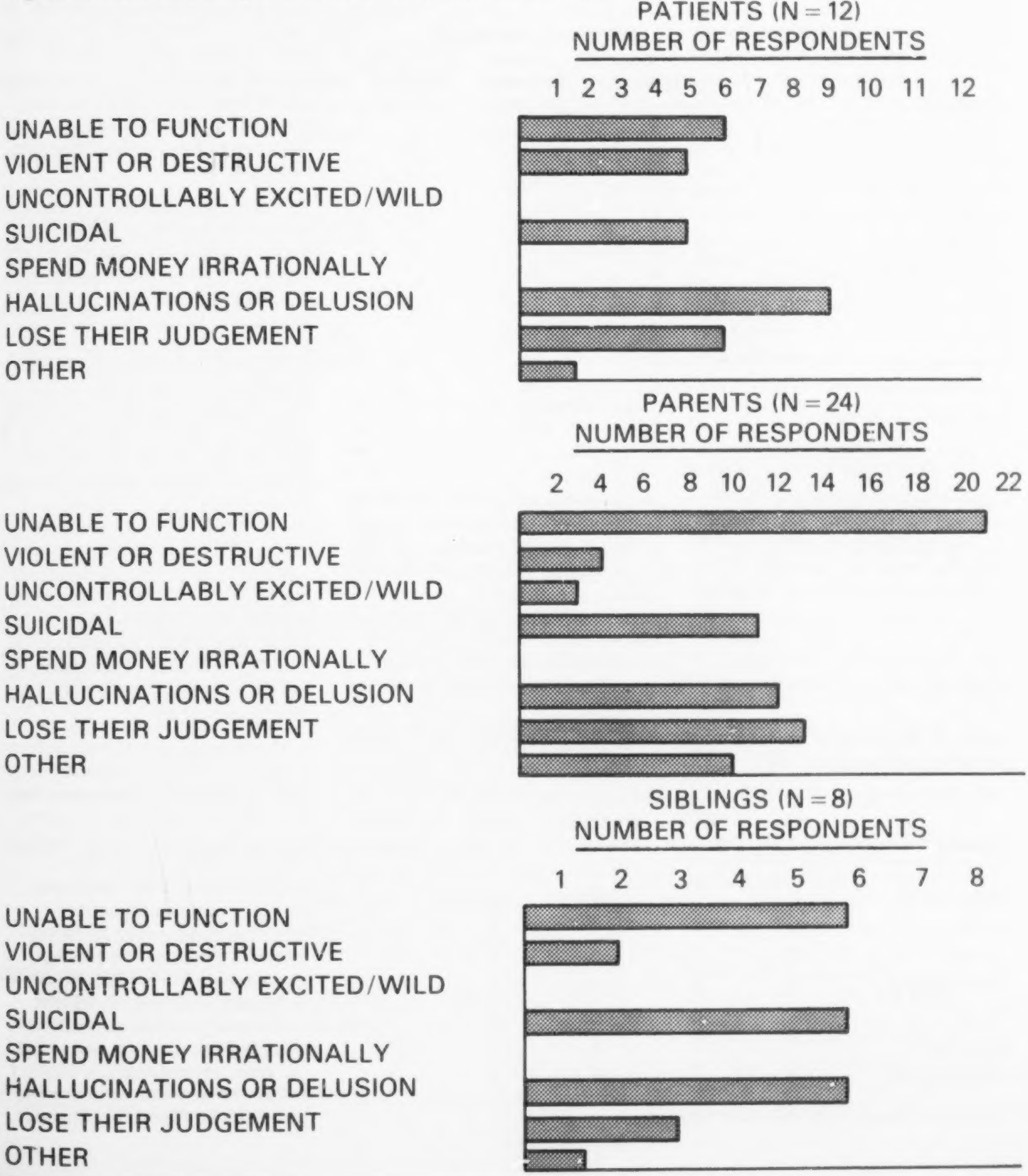


Table 5. Chronic problems and schizophrenia

Problems	Number of responses[1]		
	Patients ($n = 12$)	Parents ($n = 24$)	Siblings ($n = 8$)
Fewer jobs	10	23	8
Fears of recurrence	10	19	8
Frequent hospitalization	10	18	6
Financial strain	9	21	7
Dependence on others	9	22	7
Rejection by family/peers	8	16	5
Sexual problems	7	17	7
Child neglect	6	12	6
Trouble with law	6	8	8
Separation or divorce	5	15	3

[1] Multiple responses permitted.

again." Only 17 percent responded yes (table 8). The patients were all unmarried and had no children. When asked if they planned to have children knowing of the presence of schizophrenia in themselves, 67 percent responded that they would have children. There are obviously several possible explanations for this difference including the fact that the number of all parents who would not "do it over again" is unknown. Nevertheless, the difference in childbearing attitudes is striking. Of the sibling group, two were married and had children and six were unmarried and childless at the time of the study. When asked if they planned to have or would continue to have children knowing what they knew about schizophrenia in their family, seven of the siblings responded that they planned to have children or to have more children than they originally planned.

Table 6. Burden of different diseases as perceived by schizophrenic patients ($n = 12$)[1]

Disease	No burden	Low burden	Moderate burden	High burden	Extreme burden
Hypertension	2	5	2	3	0
Diabetes	1	4	7	0	0
Cancer	0	1	0	4	7
Heart disease	0	2	3	4	3
Mania	0	3	4	2	3
Depression	0	2	5	4	1
Schizophrenia	0	3	1	5	3

[1] Respondents asked to rate each illness separately.

To delineate further attitudes toward childbearing, a series of maximal allowable risks for development of schizophrenia in their offspring was presented to all respondents. Respondents were asked to indicate the highest risk that would not deter them from childbearing. Four of the 12 patients indicated that they would be undeterred from having children if the risk was 95–100 percent. The others would take various risks. Siblings had varied responses to the question of maximal allowable risk. The parents' responses were striking in that very few were willing to risk having an ill offspring. Mothers were more willing to take a risk than fathers (figure 4), with 7 of the 10 fathers participating in the study indicating they would take no risk at all.

The last section of the questionnaire dealt with attitudes about genetic counseling. Family members were asked what they thought of genetic counseling for schizophrenia. More than half of the respondents indicated that counseling of individuals using empirical risks would be helpful (table 9). Patients and siblings rated genetic counseling potentially harmful—33 and 50 percent, respectively—while parents saw potential harm only 4 percent of the time. Interestingly, a number of parents who did not feel schizophrenia was a heritable disorder

Table 7. Burden of different diseases as perceived by well family member (*n* = 32)[1]

Disease	No burden	Low burden	Moderate burden	High burden	Extreme burden
Hypertension	6	13	9	4	0
Diabetes	6	11	10	4	1
Cancer	2	2	2	16	10
Heart disease	0	4	9	15	4
Mania	0	1	6	14	11
Depression	0	0	9	19	4
Schizophrenia	0	0	0	7	25

[1] Respondents asked to rate each illness separately.

thought genetic counseling was a good idea.

Discussion

The respondents had a broad range of viewpoints concerning the causes of schizophrenia. The low number of parents who felt interpersonal relationships were etiologically important could be interpreted as an attempt not to see themselves as causing the illness. Whether the results of this section can be generalized for the general population of schizophrenic patients and their families is unclear as all patients and families in this study were aware of the biological nature and study goals of the unit before admission. It is unlikely, therefore, that those patients and family members who were convinced of a social or psychological etiology of schizophrenia would have sought treatment on this unit.

The assessment of prevalence was not remarkably inaccurate when the group was combined, but the patients did least well. Thus, although figures for general risk for the population are known to the researcher and clinician, they do not appear to be well known to the patient and only partially known to the families. This point is important to remember in genetic counseling.

Concerning the acute stage of the illness, the patients understandably felt that the main burden was the "positive" psychotic symptoms, whereas the parents were troubled by the negative symptoms which, one could say, put much more pressure on them as caretakers. The psychological burden of anguish and misery, although difficult to quantify, was stated dramatically by a number of the parents.

In assessing the chronic burden, all family members as a group saw the same sorts of problems for a family with a schizophrenic member. The great differences between family members focused on whether schizophrenia could ruin one's life. Less than half of the patients thought so, while 100 percent of the rest of the family did. It would be difficult for any young person to respond positively to this question, of course. The genetic counselor should keep in mind the overwhelming response of the rest of the family. It may be one reason for the reluctance of mental health care workers to discuss the diagnosis of schizophrenia openly with the patient and his family.

Schizophrenic patients say that people with schizophrenia should have children and two thirds of the patients said they plan to have children. Parents, however, felt that schizophrenics should not have children and reported in general that they would not have children if there were any risk of the offspring developing schizophrenia. The patients' siblings are more like the patients in their plans for children. Anecdotally, some sib-

Table 8. Attitudes toward childbearing

	Parents (*n* = 24)	Siblings (*n* = 8)	Patients (*n* = 12)
Would you have children?			
Yes	4 (17%)	7 (88%)	8 (67%)
No	20 (83%)	1 (12%)	4 (33%)

Probes: "Knowing what you now know about schizophrenia."
"If you had it to do over again."

lings reported that they thought of having larger families than they originally planned to make up for the possibility that the schizophrenic patient would have no children at all. This reaction has been noted previously. It has been shown for siblings of patients with Huntington's chorea and has been reported in Erlenmeyer-Kimling's (1976) "high-risk" study. As reported by other genetic counselors (Carter et al. 1971; Leonard 1972; Check 1978), it appears that the wish for children overrides considerations of risk and burden for those potentially genetically affected persons who have not reached their desired family size.

The majority of all respondents felt genetic counseling would be helpful. In its most simplistic interpretation, this may mean that a number of people would like to have the service. One should note, however, that the young people (patients and their siblings) saw potential harm to such a service although they did not elaborate on what that harm might be. If counseling services are offered to patients or siblings of patients, this fearful concern needs to be recognized.

In conclusion this study explored the views of schizophrenic patients and their families toward schizophrenia, including its etiology, prevalence, and burden. Their thoughts about implications for childbearing and genetic counseling were assessed. Generally, this group saw schizophrenia as a genetic, biochemical disorder, causing severe burden. Although there were differences in the plans of different family members which may be explained by age more than any other variable, the majority felt genetic counseling is ap-

Figure 4. Maximum allowable risk to parents

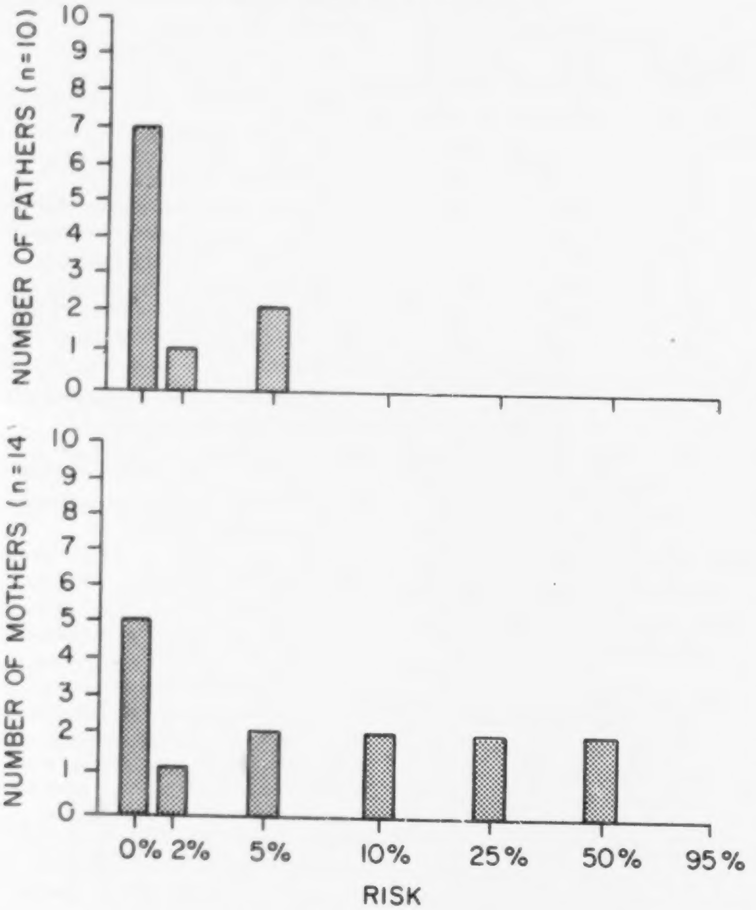


Table 9. Attitudes toward genetic counseling (in percent)[1]

Attitude	Patient (n = 12)	Parents (n = 24)	Siblings (n = 8)
Helpful	58	75	63
Necessary	25	58	38
Meaningless	17	13	13
Potentially harmful	33	4	50

[1] Multiple responses permitted. Respondents asked if counseling to assist individuals to understand the risk of occurrence of psychiatric illness in their families would be any of the above.

propriate and needed. The results demonstrate that the wish for genetic counseling exists and should be of help to those delivering the service by providing empirical data concerning the perceived burden.

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Cognitive Brain Potentials in Children at Risk for Schizophrenia: Preliminary Findings

by David Friedman,
Herbert G. Vaughan, Jr., and
L. Erlenmeyer-Kimling

Abstract

Event-related brain potentials were recorded to auditory stimuli from children at risk for schizophrenia and normal control children who were part of two independent samples being followed longitudinally. Subjects were required to detect (with a reaction time response) one of two infrequent events (either a pitch change or a missing stimulus), each of which occurred 17 percent of the time, and was embedded in a sequence of frequent events occurring 66 percent of the time. The event-related potential (ERP) elicited by both infrequent stimuli consisted of a positive-going wave peaking at 350 msec for the pitch change ERP (P350) and 400 msec for the missing stimulus ERP (P400) and a slow wave, which overlapped with and extended beyond the P350 and P400 potentials. When the eliciting event was relevant, these potentials were significantly larger than when it was irrelevant. When the waveforms produced by the high-risk (HR) subjects were compared to those produced by the normal control (NC) subjects, the HR subjects of both samples showed significantly less late positive amplitude (P350 and P400) than the NC subjects, but only when the eliciting event was relevant. This effect appeared to be independent of reaction time, as reaction time means and variances were quite similar between risk groups. Other possible explanations for this amplitude reduction were explored. Since late positive component amplitude reduction has been consistently reported to characterize the waveforms of adult schizophrenics, the reduction seen in children at genetic risk for schizophrenia may be a premorbid indicator for the development of the psychosis.

The psychophysiological functioning of adult schizophrenics has been well documented in the past two decades (see, for example, reviews by Shagass 1976; Buchsbaum 1977; Roth 1977; Shagass 1977; Venables 1977; Zahn 1977; Spohn and Patterson 1979) but it is only recently, with the advent of the high-risk longitudinal study (e.g., Mednick and McNeil 1968), that the psychophysiological functioning of their offspring has come under investigation. In this method of study, the children of schizophrenic parents are chosen as subjects because they are at greater than usual statistical risk for the development of schizophrenia (Erlenmeyer-Kimling 1968; Zerbin-Rüdin 1967).

The tasks and stimulus parameters used with these children have come from those used with adult schizophrenics since, if it is assumed that the disorder is, at least in part, genetically determined, a dysfunction found in the adult might also be demonstrable in the child at genetic risk.

One of the most consistent event-related potential (ERP) findings with adult schizophrenics has been the reduction, relative to controls, in late positive component (P300) amplitude (Roth and Cannon 1972; Levit, Sutton, and Zubin 1973; Verleger and Cohen 1978;

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Timsit-Berthier and Gerono 1979; Pass et al. 1980; Roth et al. 1980*a*, 1980*b*), a brain potential whose relationship to cognitive processing has been repeatedly and powerfully demonstrated (cf. Donchin, Ritter, and McCallum 1978). A second, long-latency, cognitive-related component, slow wave, has also been shown to be reduced in adult schizophrenics relative to normal controls and psychotically depressed patients (Roth et al. 1981). The middle-latency components, N100 and P200, have also been reported to be reduced in schizophrenics (Shagass 1976; Buchsbaum 1977; Lifshitz et al. 1979; Pfefferbaum et al. 1980; Roth et al. 1980*a*). Since N100 and P200 amplitudes increase with increments in level of attention (e.g., Picton and Hillyard 1974; Hillyard et al. 1978), these data suggest the presence of an attentional dysfunction in the adult schizophrenic. While the endogenous (cognition-related) and exogenous (stimulus-elicited) potentials are reduced in schizophrenics relative to normals, the early brainstem responses do not differ between these groups (Pfefferbaum et al. 1980), indicating that peripheral factors cannot account for the abnormalities that have been reported for the later portions of the schizophrenics' ERP waveform.

Any one of the ERP differences between schizophrenics and controls may be a consequence of the disturbances in mental functioning produced by the psychosis, rather than a true premorbid indicator. Furthermore, since the various components in the ERP waveform reflect different aspects of information processing, it is to be expected that each might have differential importance as indices of potential psychopathology. Thus, discrepancies that are evident across studies in precisely which components are reduced or enhanced in schizophrenic patients relative to controls should be clarified through the longitudinal following of children at risk for schizophrenia, since the objective of the psychophysiological aspects of this research is to obtain patterns of ERP response that are predictive of the development of the psychosis.

In the behavioral domain, reaction time slowing in schizophrenics relative to controls is one of the most consistently reported findings (cf. Nuechterlein 1977). Since P300 latency and reaction time covary under some conditions (Ritter, Simson, and Vaughan 1972; Kutas, McCarthy, and Donchin 1977; Friedman, Vaughan, and Erlenmeyer-Kimling 1978; Ritter et al. 1979), the reduced amplitude P300 seen in schizophrenics could be due to longer and more variable latency of the single-trial potentials that comprise the averaged response. To determine if this is the case, ERPs and reaction times must be recorded concurrently. Although little used in schizophrenia research, this methodology is powerful as both cognitive deficits and impaired physiological responsiveness have been reported to characterize these disorders. (See, for example, Chapman (1979) for a review of the cognitive area; and Spohn and Patterson (1979) for a review of recent ERP findings.)

This methodology allows the investigator to determine under which circumstances behavioral and physiological measures are or are not related and to what extent deficits in either domain are more severe in acute psychotic states. For example, Roth et al. (1980*a*) simultaneously recorded ERPs and reaction times in schizophrenics and controls and found reduced P300 amplitude and longer reaction times in the schizophrenics. However, P300 latency was identical in the two groups. Since latency of this component has been associated with stimulus evaluation time (cf. Donchin, Ritter, and McCallum 1978), these data suggested that response organization rather than stimulus evaluation was delayed in the schizophrenics. Several control analyses (reported in Roth et al. 1980*b*) showed that the reduction in P300 amplitude was not due to the longer and more variable reaction times recorded from the schizophrenics. None of these conclusions could have been reached without concurrent recording of the two measures.

Since cognitive and attentional disturbances are reported to characterize some high-risk children (e.g., Garmezy 1978; MacCrimmon et al. 1980; Cornblatt and Erlenmeyer-Kimling, in press; Erlenmeyer-Kimling et al., in press; Nuechterlein et al., in press), the simultaneous recording of ERPs and behavioral measures could be potentially useful when applied to high-risk samples. However, few studies using this research tactic with high-risk children have been published. We (Friedman, Vaughan, and Erlenmeyer-Kimling 1979) did not find significant mean group differences when visual ERPs were recorded from high-risk and normal control children during two versions of a visual continuous performance test that differed in their processing complexity. However, of 30 high-risk and 30 normal control subjects, a subgroup of four high-risk children were flagged, who differed from the remainder of the high-risk and normal control groups in showing small, between-task differences in late positive component amplitude. In the normal subjects and the remainder of the high-risk group, the more complex task elicited larger late positivity, indicating that reduced late positive activity may characterize at least some high-risk children.

For the current study, we designed an experiment in which we could record ERPs and behavioral responses simultaneously. The task was a modification of paradigms which had been shown to produce reduced late positive component amplitude in adult schizophrenics relative to controls (e.g., Roth et al. 1980*a*, 1980*b*). Its processing requirements ensured that we would record P300 and slow wave (SW), brain potentials thought to reflect cognitive information processing (cf. Donchin, Ritter, and McCallum 1978). Using a task that had produced amplitude differences between adult patients and controls should have maximized our chances of obtaining the same amplitude reduction in children at genetic risk. If we found reduced amplitude late positivity in high-risk children, who do not display any overt symptomatology, this would suggest that the reduction is a true premorbid indicator and not simply a consequence of the disturbances in mental functioning produced by the schizophrenic psychosis.

Methods

Subject Selection and Parental Diagnoses. For this preliminary analysis of the auditory ERP, data are included on the first 56 children (28 high-risk subjects = HR; 28 normal control subjects = NC) from our initial cohort who came for their third round of testing (sample A3) and on the first 30 children (n = 13 HR; 17 NC) from our second cohort (sample B1). Sample B1 provides a replication for sample A. A detailed description of the samples and the study as a whole appears in Erlenmeyer-Kimling et al. (in press).

In both samples, the children of mentally ill parents were ascertained through the admission of the parent to one of several state psychiatric facilities in the New York Metropolitan area. As an initial diagnostic evaluation, records of these patients were reviewed blindly and independently by two psychiatrists. For sample A, each of the reviewers assigned a diagnosis based on the record materials using *DSM-II* criteria, completed a symptom checklist, and scored the 100-point Global Assessment Scale (Endicott et al. 1976) assessing the severity of impairment. Only those cases for which there was full diagnostic agreement were retained for study. For sample B, in addition, Research Diagnostic Criteria (Spitzer, Endicott, and Robins 1975) were used in the initial diagnostic evaluation.

In sample A, the NC group was obtained with the cooperation of two large school systems. For sample B, a population sampling firm was used to conduct a survey for the purpose of obtaining demographic information on a large number of families, which then formed a pool from which matches (based on socioeconomic level, age, and sex of the children) from the sample B HR subjects could be drawn. In both samples A and B, families were excluded from the NC group if either parent was found to have had psychiatric treatment.

In this preliminary analysis of the data, children of parents with affective psychoses were not included, due to the extremely small number of subjects falling into that category at the time these analyses were performed. Demographic characteristics of the two samples are presented in table 1. In order to be included, all families had to be intact. The age range of subjects from sample A was 11 to 18 and for sample B was 10 to 12.

Task Procedures and Stimuli. The task was designed to obtain ERPs to relevant, irrelevant, and background auditory events. During each block of trials, the children heard three kinds of events: a frequent tone pip (1000 Hz, 64 dB SPL), which occurred 66 percent of the time, a pitch change from the standard frequency (PC at 700 Hz, 64 dB SPL), and a stimulus omission or missing stimulus (MS). PC and MS each occurred 17 percent of the time. The stimuli (50 msec duration, 2.5 msec rise and fall times) were presented binaurally over headphones (TDH-39), with an interstimulus interval of 800 msec. Subjects were instructed to respond with a finger lift (which activated a reaction time key of local design) to one of the infrequent

Table 1. Characteristics of the high-risk and normal control samples

	A3		B1	
Sample	**HR**	**NC**	**HR**	**NC**
# SM	18	—	11	—
# SF	5	—	1	—
# Both	2	—	1	—
# Mixed	3	—	—	—
Mean age	15	14.4	10.8	11.4
SD	1.7	1.8	.72	.86
# Male	18	16	5	9
# Female	10	12	8	8
Totals	28	28	13	17

Abbreviations: SM = schizophrenic mother; SF = schizophrenic father; Both = both parents schizophrenic; Mixed = one parent schizophrenic, one parent affective; HR = high risk; NC = normal control.

events, with the stimulus which was relevant alternated across four blocks of trials for a total of 300 stimuli per block. A finger lift within the interval of 200–1000 msec after the onset of each relevant stimulus was considered a correct response, while a lift at any other time was counted as an error.

Data Acquisition and Recording Procedures. EEG was recorded from Beckman Biopotential electrodes located at midline frontal (Fz), central (Cz), parietal (Pz), and occipital (Oz) scalp sites, and vertical EOG was recorded from an electrode located above the right eye. All leads were referred to the right earlobe. The physiological signals were amplified on an eight-channel Beckman Dynograph Type RM recorder with Type 481B preamplifiers and Type 482MB amplifiers with a time constant of 1 second and high frequency cutoff at 30 Hz.

Data acquisition and stimulus presentation were under the control of a PDP 11/10 computer, which digitized the physiological data at 4 msec intervals for a 100 msec prestimulus and a 700 msec poststimulus epoch and recorded it, along with reaction time, on nine-track digital tape. Trials containing movement and/or eye artifact were rejected and not included in the averaged responses.

Data Analyses

Averaging. The design of the experiment allowed the averaging across blocks of ERPs to the physically identical stimulus when relevant and when irrelevant, yielding four averages per subject. Ideally, there was a total of 102 PC and MS when relevant and the same number when irrelevant. Eye and other movement artifacts, as well as omission and commission errors (a response to the irrelevant event), reduced these numbers in most subjects. The number of ERP epochs per average varied from 14 to 99 for PC relevant; from 28 to 99 for PC irrelevant; from 12 to 94 for MS relevant; and from 21 to 98 for MS irrelevant. There were no significant differences between HR and NC groups in the number of epochs comprising the averages in either sample A3 or sample B1.

Base to peak measures. For each subject, measures of P350, P400, and SW amplitudes were obtained using the average amplitude over the 100 msec preceding stimulus onset as a baseline. The amplitude measure for each component was computed as the average amplitude over 100 msec centered about the peak of the factor loadings associated with that component and for SW was taken as the average amplitude corresponding to the 100 msec when the SW factor loadings were at their greatest (see below).

Principal components analysis (PCA). ERP components are known to overlap at the scalp. For example, two components with temporally adjacent peaks may summate with a peak latency intermediate to the two original components. This leads to error when attempting to estimate peak amplitude values by visual inspection since the measurement of one component may be contaminated by an unknown contribution from the amplitude of adjacent or overlapping components. PCA has been used quite successfully by ERP investigators to disentangle these overlapping components; see, for example, Donchin and Heffley (1978) for an explanation of PCA in an ERP context. Since P300 and SW are known to interact in this manner (e.g., Squires, Squires, and Hillyard 1975;

Squires et al. 1977; Ruchkin et al. 1980), PCA was used to obtain measures of these potentials uncontaminated by overlap. An added advantage of this method in the study of clinical samples, as in the current report, is that it permits rigorous and objective definitions of components, producing factor score measures of ERP activity without any subjective bias which might occur when hand scoring the data.

The factors which result from the PCA are statistical representations of "peaks" in the original waveforms. A high factor loading indicates a high correlation between the factor and the voltage of the scalp potential at a given point in time. Each factor can then be associated with voltage peaks that are active in different time regions in the original ERP waveforms. The amplitude of each of the peaks in a given subject's waveform can then be expressed using the factor score.

Since amplitude of a given component might distinguish the groups, the cross-products matrix was factored. No transformations are performed on the data when using this association matrix (Glaser and Ruchkin 1976; Donchin and Heffley 1978), thus retaining the original microvolt scale and amplitude information present in each subject's waveform.

Because the factors are statistical representations of components in the original ERPs, it was important to verify that the ERPs from each risk group produced similar factor loading functions and factor structures. This would provide a measure of reliability and allow the pooling of the data across risk groups in order to enter between-groups variance into the analysis. For each of these initial analyses, PCA was performed separately on the ERPs elicited by the PC (relevant and irrelevant) and the MS (relevant and irrelevant) for the NC and HR groups of each sample. Thus, there were 8 PCAs (2 stimuli—MS, PC; by 2 risk groups—HR, NC; by 2 samples—A3, B1). PCA was performed using 66 time points (at 12 msec per point) as "variables" and the waveforms as "cases." For all analyses, the number of cases entered was 2 (relevant/irrelevant) by 4 (electrode locations) by number of subjects, yielding 224 waveforms for the HR and NC groups in sample A3, with 28 subjects per group, and 104 waveforms for the HR subjects of sample B1 (with 13 subjects) and 136 waveforms for the NC group of B1 (with 17 subjects). For the pooled groups PCAs, the number of cases entered was 448 for A3 and 240 for B1.

In order to determine if the factors derived from these separate PCAs of the PC and MS of each risk group and sample represented the same brain activity, the factor scores for each extracted component were subjected to Relevance (relevant/irrelevant) by Electrode location (Fz, Cz, Pz, Oz) repeated measures analysis of variance (ANOVA) (BMDP2V; Dixon 1975). If each factor (for example, P300 factor of HR B1 compared with P300 factor of NC B1) showed similar scalp distribution and relationship to the variables of relevance, electrode location and their interaction, we concluded that each represented the same brain potential in each set of data.

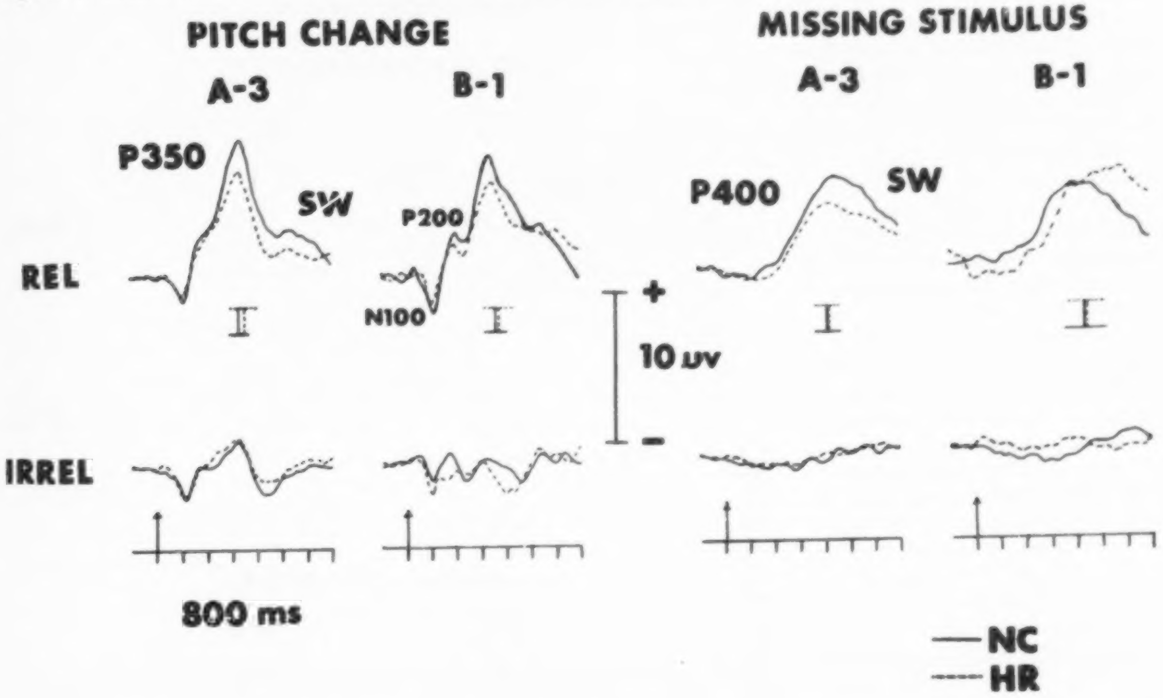
For the pooled groups analyses, the factor scores were subjected to Group (NC/HR) by Relevance (relevant/irrelevant) by Electrode location (Fz, Cz, Pz, Oz) ANOVAs with repeated measures on the last two variables. For purposes of the present report, only the results of the P300 and SW factors will be reported.

Statistical significance. Because of the empirically based expectation that only a small percentage of HR children will eventually manifest schizophrenia, it is unlikely that large group differences will occur (see, for example, Hanson, Gottesman, and Heston 1977; Friedman, Frosch, and Erlenmeyer-Kimling 1979). However, it is probable that a small group of deviant subjects could produce a trend toward significance or a marginally significant effect that, if overlooked, would lead to a Type II error (false negative), or the conclusion that parental diagnosis had no effect when, in fact, it did. Therefore, our criterion for statistical significance was set at 0.10.

Results

ERP Waveforms. The grand mean ERPs recorded at the parietal electrode, averaged across subjects within each risk group and sample, to the relevant and irrelevant infrequent events are depicted in figure 1. ERPs associated with the infrequent event contained a large-amplitude late positivity-slow wave complex, which was larger for the relevant than for the irrelevant event. For the PC ERP, this positivity peaks at 350 msec poststimulus and is labeled P350, while for the MS it peaks at 400 msec. These endogenous late positive potentials, although of different latencies, are

Figure 1. Grand mean ERPs recorded from the parietal electrode



The ERPs have been averaged across subjects from each risk group and sample in response to the two infrequent events when relevant and when irrelevant. Arrows denote stimulus onset with time lines every 100 msec. Mean reaction time is indicated by vertical bars with plus and minus one standard deviation marked by horizontal bars. REL = relevant; IRREL = irrelevant; SW = slow wave.

identified with the classical P300 component. SW activity, which overlaps with and extends beyond P350 and P400 components, is also evident. In addition, the PC ERPs are composed of the exogenous potentials, N100 and P200, which are not present in the brain potentials elicited by the absence of stimulation.

The morphology of the ERPs elicited by both events is remarkably consistent among NC and HR groups of both samples. The most striking difference between HR and NC waveforms occurs when the eliciting event is relevant. The HR subjects of both samples show a reduction in late positivity relative to NC subjects. For A3, this reduction comprises P350, P400, and SW amplitudes, while for B1 it holds only for P350 and P400 amplitudes. For SW, the opposite occurs, greater amplitude for HR than NC subjects of B1 for both PC and MS ERPs.

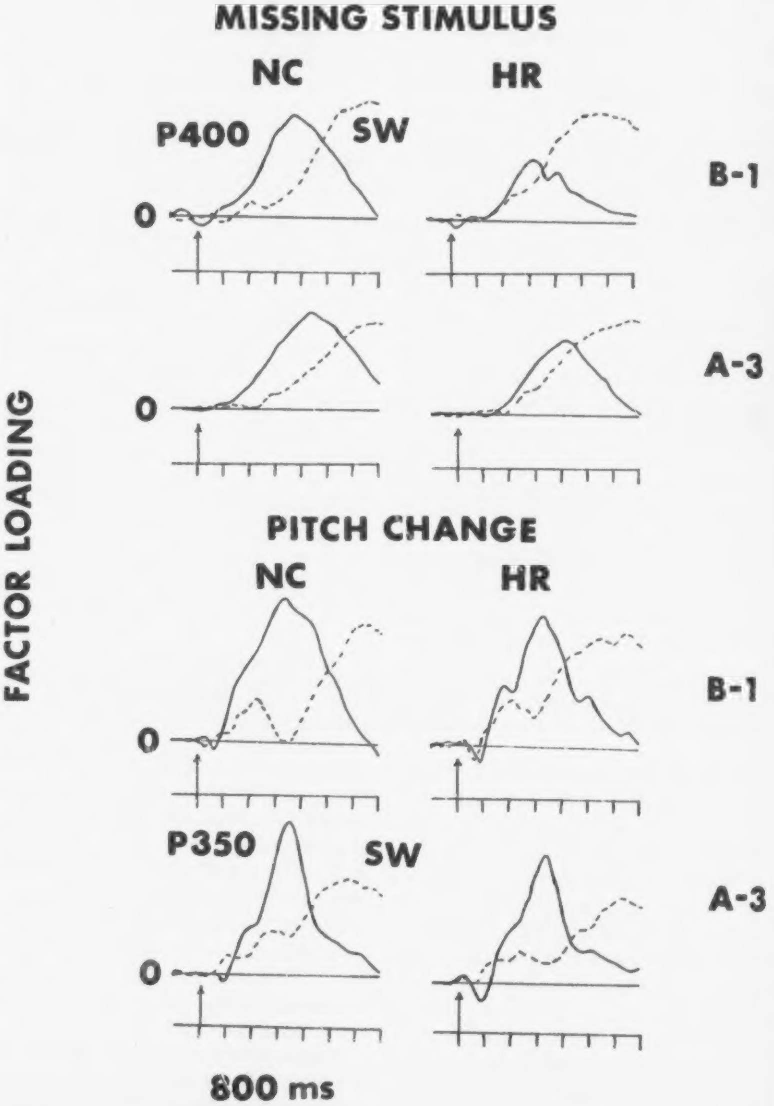
Mean reaction time (RT) and its associated variability are both greater for the MS than for the PC, but are quite similar when the comparison is made between risk groups of each sample.

Base to peak measures. For the PC ERP, P350 amplitude was computed as the average amplitude over 300 to 400 msec poststimulus, and for the MS ERP, P400 amplitude was computed as the average amplitude over 350 to 450 msec poststimulus. For both PC and MS ERP, SW amplitude was computed as the average amplitude over a 100 msec epoch beginning 600 msec after stimulus onset. This corresponded, for both risk groups and samples, to the times when the factors associated with these components had their maximum loadings (see PCA analyses below).

Group (HR/NC) by Relevance (relevant/irrelevant) by Electrode location (Fz, Cz, Pz, Oz) ANOVAs were performed separately on the PC and MS base to peak measures for each sample, and these results were essentially identical to those using the factor score measures of ERP activity. Therefore, only the results of the ANOVAs using the PCA measures will be reported in detail.

Statistical Representation of the Waveforms. Figure 2 depicts the varimax-rotated factor loading functions obtained from PCAs of the cross-products matrix performed separately on the PC and MS ERPs for each risk group (HR versus NC) and sample (A3 and B1), yielding eight PCAs. With one exception (MS for HR group of sample B1), P300 and SW were always the first two factors extracted. Table 2, which presents the percentages of variance accounted for by each factor, shows that in each analysis the late positivity-SW complex accounted for at least 75 percent of the variance. For the MS, the factor loadings depicted with solid lines have the same shape and peak at approximately the same time as P400 depicted in figure 1. Thus, this factor is associated with P400 in the original data. The second factor, depicted with dashed lines, has high positive loadings in the very late portions of the epoch and is, therefore, associated with SW in the original waveforms. For the pitch change ERPs, the solid-line factors have similar shape and latency to peak as P350 in the original waveforms and are, therefore, associated with that component. As in the MS factors, the dashed lines represent SW activity, since they are active in the very late portion of the recording epoch when P350 is returning to baseline

Figure 2. Varimax rotated factor loading functions obtained from the within-groups cross-products matrices



The PCAs were performed separately on the PC and MS ERPs within each risk group and sample. Solid lines represent P350 (PC ERP) and P400 (MS ERP) components in the original data, while the dashed lines represent slow wave (SW) activity in the original waveforms. Arrows denote stimulus onset with time lines every 100 msec.

Table 2. Percentage of variance of late positivity–slow wave complex in both groups and samples for within-groups PCAs

	Stimulus			
	PC		MS	
	Factor		Factor	
Sample	P350	SW	P400	SW
B1				
HR	13	65	13	71
NC	59	19	18	68
A3				
HR	61	15	11	75
NC	62	13	75	10

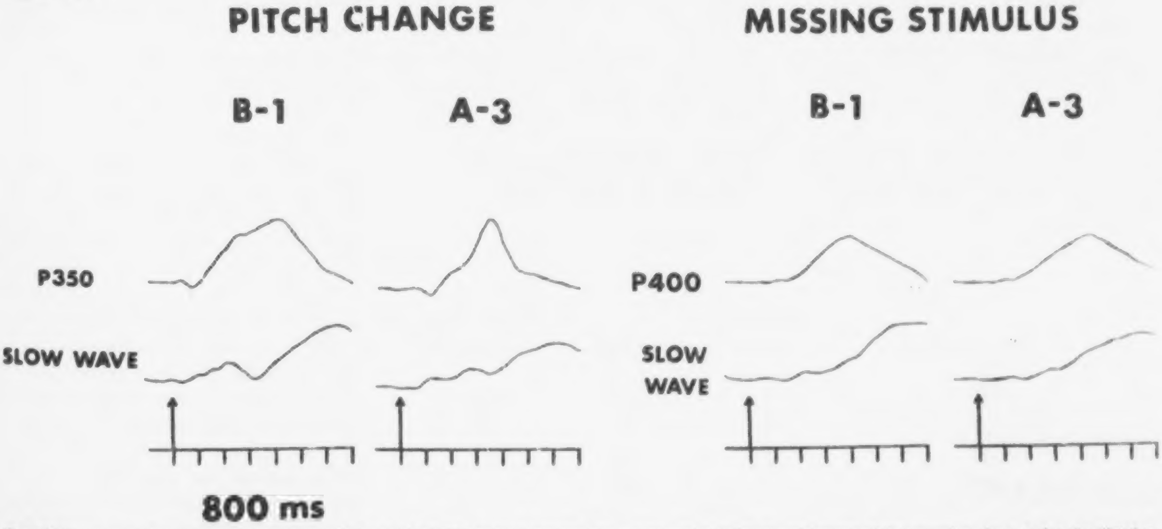
Abbreviations: PC = pitch change ERP; MS = missing stimulus ERP; HR = high risk; NC = normal control.

in the original ERPs.

ANOVAs (Relevance by Electrode location) of the factor scores, performed separately for the MS and PC, support the conclusion that the factor associated with late positivity and the factor associated with SW represented the same brain potentials in each of the eight data sets. In all analyses, P350 and P400 factors were both maximal at the parietal electrode, while SW was negative frontally and positive parietally. For all ANOVAs P350 and P400 factors showed main effects of Relevance and Electrode location and strong interactions of Relevance and Electrode location.

Since the components extracted from the separate PCAs were shown to be the same for HR and NC groups of both samples, we pooled the ERP of HR and NC groups (maintaining separateness of each sample), thus allowing between-group variance to enter the PCA. The rotated factor loadings from these analyses appear in figure 3. Again, the late positivity-SW complex accounted for at least

Figure 3. Varimax rotated factor loading functions obtained from the between-groups cross-products matrices



The PCAs were performed separately on the PC and MS ERPs pooled across risk groups maintaining separateness of the samples. Arrows denote stimulus onset with time lines every 100 msec.

75 percent of the variance (table 3) and, as can be clearly seen, the factors are highly similar to those based on the within-groups analyses.

Factor Score Analyses. The mean factor scores (obtained from the pooled groups analyses) averaged across subjects within each group and sample are presented in figure 4, and the significance of the depicted trends as assessed by Group (HR/NC) by Relevance (relevant/irrelevant) by Electrode location (Fz, Cz, Pz, Oz) ANOVAs are shown in table 4.

Effects not involving risk group. Electrode location was a significant source of variation in all analyses. As can be seen in figure 4, SW was negative frontally and positive at the parietal electrode, as previously reported for this long-latency factor (e.g., Squires, Squires, and Hillyard 1975; Squires et al. 1977), while P350 and P400 showed parietal maxima, also in agreement with previous reports for this late positive activity (e.g., Hillyard et al. 1976; Simson, Vaughan, and Ritter 1977; Friedman, Ritter, and Simson 1978). P350 and P400 produced highly significant Relevance main effects in both samples, with the relevant event producing greater amplitude than the irrelevant event. For these two components, the Relevance by Electrode location interactions were shown by tests for simple effects (Winer 1971) to be due to greater mean differences between relevant and irrelevant at Pz and Oz than at Fz and Cz (all Fs for sample A3 > 3.50, $df = 1, 162$, $p < .10$ or less; all Fs sample B1 > 8.00, $df = 1, 84$, $p < .01$ or less), and to steeper amplitude gradients across the scalp for relevant than for irrelevant P350 and P400 components (all Fs sample A3 > 8.70, $df = 1, 162$, $p < .005$ or less; all Fs sample B1 > 5.90, $df = 1, 84$, $p < .05$ or less).

Group effects. The factors representing P400 and P350 brain activity showed interactions of Electrode location with Risk Group (with the exception of the PC for sample A3). For the PC ERP, these interactions were due primarily to small, nonsignificant between-group differences at Fz and Cz, with larger, significant differences favoring the NC group at Pz (all Fs sample A3 > 2.60, $df = 1, 162$, $p < .10$ or less; all Fs sample B1 > 2.97, $df = 1, 84$, $p < .10$ or less). A different pattern was obtained for sample B1's P400 factor, where the HR group produced significantly greater P400 amplitude than the NC subjects at Fz and Cz (Fs > 3.00, $df = 1, 84$, $p < .10$ or less), with no differences at Pz. Reference to figure 4 shows that for SW the significant Electrode location by Group interaction for A3's PC occurred because the HR group produced SWs which were more negative at the two anterior electrodes than the NC group's, producing steeper topographic gradients for the HR subjects (Fs > 19.00, $df = 3, 162$, $p < .001$ or less).

Table 3. Percentage of variance of late positivity–slow wave complex in both samples from the between-groups PCAs

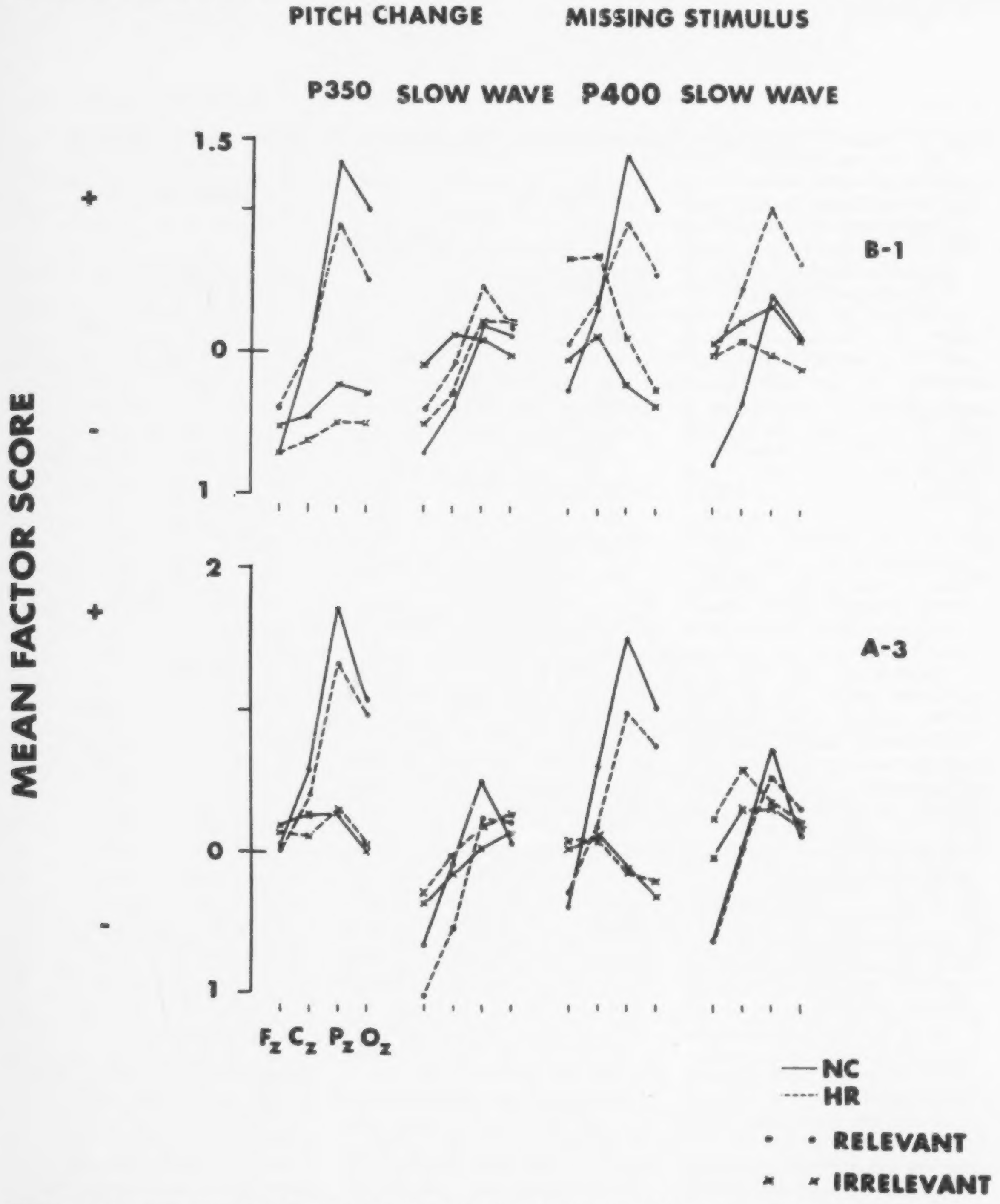
		Sample			
		A3		B1	
Stimulus	Factor	Percent	Cumulative percent	Percent	Cumulative percent
PC	P350	61	61	62	62
	SW	15	76	16	78
MS	P400	10	10	15	15
	SW	75	85	69	84

Abbreviations: PC = pitch change; MS = missing stimulus.

For B1, the significant Relevance by Group interaction for the MS SW occurred because the HR subjects produced greater SW than the NC subjects when the event was relevant ($F = 3.9$, $df = 1, 27$, $p < .10$), with no difference between groups when the MS was irrelevant.

The two significant triple interactions occurred for sample B1 and only for the PC factors. For P350, this interaction was caused by the HR subjects showing significantly greater relevant P350 amplitude at the frontal electrode than the NC group, but significantly less amplitude than the NC group at the parietal electrode (Fs > 5.2, $df = 1, 84$, $p < .05$ or less), while for irrelevant P350, the NC subjects showed significantly greater amplitude than the HR subjects, but only at the parietal site ($F = 4.06$, $df = 1, 84$, $p < .05$). For SW, the triple interaction was due to the HR subjects producing significantly greater SW than the NC subjects

Figure 4. Factor scores obtained from the pooled groups PCAs corresponding to P350, P400, and SW factors depicted in figure 3



Scores have been averaged across subjects in each risk group and sample and are plotted for relevant and irrelevant events at each of the 4 electrode sites (Fz, Cz, Pz, Oz).

Table 4. *F* ratios from Group by Relevance by Electrode location ANOVAs for samples A and B

	Sample A3			Sample B1		
	Pitch change					
	Factors			Factors		
Source	*df*	P350	SW	*df*	P350	SW
Group (G)	1/54	.46	.20	1/28	.71	.14
Relevance (R)	1/54	45.96****	1.20	1/28	27.07****	.15
RG	1/54	.91	1.11	1/28	.07	.74
Electrode location (L)	3/162	50.20****	39.31****	3/84	46.20****	14.71****
LG	3/162	.81	2.60*	3/84	2.85*	1.06
RL	3/162	83.71****	8.74****	3/84	39.46****	3 .60*
RLG	3/162	1.53	1.13	3/84	3.30*	2.55*
	Missing stimulus					
	Factors			Factors		
	df	P400	SW	*df*	P400	SW
Group (G)	1/54	.49	.42	1/28	.48	1.65
Relevance (R)	1/54	30.81****	1.80	1/28	5.99*	.27
RG	1/54	.96	.64	1/28	2.33	3.74*
Electrode location (L)	3/162	38.09****	26.65****	3/84	7.03****	18.73****
LG	3/162	2.40*	.96	3/84	5.78***	1.10
RL	3/162	74.52****	12.45****	3/84	32.78****	16.31****
RLG	3/162	1.54	.26	3/84	.39	.85

*$p < .1/.05$; ** $p < .01$; *** $p < .005$; **** $p < .001$.

at all four electrode locations when the PC was relevant (*Fs* > 4.00, *df* = 1, 84, $p < .05$ or less), but significantly less SW amplitude when the event was irrelevant, but only at Fz and Cz (*Fs* > 5.5, *df* = 1, 84, $p < .025$ or less).

Analysis of deviant subjects. We inspected the distributions for P300 and SW at each electrode site for both samples to determine if there were HR subjects at the tails who could have been responsible for producing the small group differences that we observed. While in a few cases (most notably for the SW recorded at the frontal electrode), there were a small number of HR subjects with extreme scores, in the remaining instances it looked as if the majority of HR subjects were characterized by the reduced amplitude, leading to the small group effects that we observed.

Analyses of the Behavioral Data. With the exception of reaction time, analyses of behavioral responses were based upon the entire sequence of trials, including those that were rejected for purposes of obtaining artifact-free ERP averages. The number of correct detections of the PC and MS, the number of irrelevant stimuli responded to (i.e., responding to the PC when the MS was relevant), and the number of standards responded to were analyzed with Group (HR/NC) by Stimulus (PC/MS) repeated measures ANOVAs. The MS was the more difficult of the two stimuli to detect; when it was relevant, it produced significantly more errors (misses, responses to the irrelevant event, and responses to the standard) than the PC (all Fs sample A3 > 6.10, $df = 1, 54$, $p <$ .01 or less; all Fs sample B1 $>$ 11.20, $df = 1, 28$, $p < .002$ or less), with the exception of responses to the standard for A3, where no differences between stimuli were noted. For B1, no Group or interaction effects were observed. For A3, there was a significant Group by Stimulus interaction for number of correct responses ($F = 4.43$, $df =$ 1, 54, $p < .04$). While the NC group detected the same mean number of PCs and MSs (mean number PCs = 86.30, SD = 18; mean number of MSs = 85.40, SD = 11), the HR group detected significantly more PCs than MSs (mean number of PCs = 90.4, SD = 12; mean number of MSs = 79.90, SD = 16) ($F = 9.74$, $df = 1, 54$, $p < .005$), with no differences between the groups.

Reaction times to the relevant events were analyzed in the same manner. Response latency was significantly longer to the MS than the PC in both samples (F sample A3 = 91.00, $df = 1, 54$, $p < .001$; F sample B1 = 64.00, $df = 1, 28$, $p <$ .001), with no Group main or interaction effects. Within-subject reaction time standard deviations were greater to the MS than the PC in both samples (F sample A3 = 84.00, $df = 1, 54$, $p < .001$; F sample B1 = 28.64, $df = 1, 28$, p $< .0001$), but neither the main effect of Group nor the interaction of Group and Stimulus were significant for either sample.

Discussion

We have shown in two independent samples that late positive activity (P350, P400, and SW) elicited by infrequent, relevant events is significantly reduced in the HR children's waveforms relative to those recorded from normal control subjects. This reduction in late positivity is one of the most consistently reported findings when ERPs are recorded from adult schizophrenics (Levit, Sutton, and Zubin 1973; Shagass 1976; Verleger and Cohen 1978; Timsit-Berthier and Gerono 1979; Pass et al. 1980; Roth et al. 1980*b*), suggesting that this amplitude reduction may be a premorbid indicator for the development of schizophrenia.

Functional Roles of P300 and SW. Before the various factors that might account for the finding of reduced positivity in the HR waveforms are discussed, a brief summary of the possible functional role(s) of P300 and SW follows. Although P300 latency can be highly correlated with reaction time, it cannot index the decision to respond, as its peak occurs after that decision has been made (e.g., Ritter, Simson, and Vaughan 1972; Kutas, McCarthy, and Donchin 1977; Friedman, Vaughan, and Erlenmeyer-Kimling 1978; Ritter et al. 1979; Towey et al. 1980). Thus, its functional role has to be related to mental processes (not necessarily conscious) occurring after the discriminative decision. Although the matter is by no means definitively settled, current theorizing and experimental evidence suggest that P300 may reflect processes related to the preparation for future events. These psychological processes may include memory registration, strategy updating, or other, equally likely constructs, and have been referred to collectively as "contextual updating" functions (cf. Donchin, Ritter, and McCallum 1978). The fact that SW amplitude has been enhanced in tasks requiring the subject to engage in strategies that necessitate cognitive processing long after the decision to respond has been made (e.g., Ruchkin et al. 1980) suggests that it too may have a role in the updating process (see also Sutton and Ruchkin 1980). However, this functional interpretation of the P300-SW findings has been inferred from the data; a direct test of the contextual updating hypothesis has not been made. Thus, while still uncertain, it is plausible that the P300-SW complex could reflect brain activity related to these kinds of processes.

P300 Reduction-Latency Variability. With this possible functional role in mind, P300 amplitude reduction may be caused by many factors. Differences in P300 amplitude in averaged ERPs can be due to latency variability in the single trials that comprise the average. Since P300 latency covaries with reaction time under some conditions (e.g., Ritter, Simson, and Vaughan 1972; Kutas, McCarthy, and Donchin 1977; Friedman, Vaughan, and Erlenmeyer-Kimling 1978; Roth, Ford, and Kopell 1978), the reduction seen in the HR children could be due to greater variability in their reaction time distributions, which could indicate greater latency variability in the single trials of these subjects in comparison to the NC subjects. However, the fact that mean reaction time and its associated variability to both infrequent events were quite similar in both groups from both samples mitigates against this explanation.

P300 amplitude could also be reduced by single trial variability which does not covary with reaction time. This source of variation can be assessed using adaptive filtering (Woody 1967), which uses the peak of P300 as the reference point for averaging (the resulting average is referred to as "latency compensated") (Ruchkin and Sutton 1978). If P300 amplitude is enhanced by the application of the filter, this indicates that latency jitter of P300 in single trials has reduced the amplitude in the conventional, stimulus-locked average. Although it is unlikely that RT-independent variability in P300 latency causes the reduced P300 amplitude in HR subjects, the extent to which latency jitter contributes to this effect should be directly evaluated.

Roth et al. (1980*b*) eliminated reaction time and latency variability as causative of P300 reduction in their adult schizophrenic sample. P300 amplitude was not normalized either by obtaining averages synchronized with the reaction time response (thus reducing reaction time variability), or by application of the Woody filter (reducing single trial latency variability). Thus, in the adult schizophrenic, P300 is reduced in amplitude in single trials. Together with the reaction time analyses of the current report, these data suggest that P300 reduction in the HR children's ERPs is also due to amplitude differences occurring in the single trial.

Roth, Ford, and Kopell (1978) and Friedman (1981) have shown that SW grows in amplitude as reaction time and its variability increase. For the A3 HR subjects, SW was significantly reduced compared to the NC children, again arguing against reaction time variability as a determinant of the amplitude loss. However, the B1 HR subjects produced enhanced SW relative to controls, presenting a more complicated picture for this waveform in the two HR samples. Since the B1 HR subjects are younger than those of A3, these SW differences could be due to the age differential between the two samples. In support of this notion, preliminary data (Friedman, unpublished observations) demonstrate larger SW in the ERPs of the youngest subjects tested.

P300 Reduction—Subjective Probability and Task Relevance. The usual interpretation of smaller P300s is that the stimuli that elicited them were less task relevant or had a higher subjective probability or expectancy (e.g., Duncan-Johnson and Donchin 1977; Roth et al. 1976; Squires et al. 1976; Johnson and Donchin 1980). Since RT was similar in both groups, it would be difficult to consider the reduced amplitude as indicating that the infrequent stimuli were treated as less task relevant by the HR than by the NC subjects. It seems more likely that the deficit lies in not perceiving the probabilities accurately. There is a systematic increase in P300-SW amplitude elicited by an event depending upon the number of repetitions of a different event that preceded it (Squires et al. 1976; Johnson and Donchin 1980). If some HR subjects do not form accurate representations of the sequential probability of the stimulus train, this might be one way in which P300 amplitude is reduced in these subjects.

Certainly, cognitive and/or attentional disturbances, which have been reported to characterize some high-risk children (e.g., Asarnow et al. 1977; Rutschmann, Cornblatt, and Erlenmeyer-Kimling 1977; Garmezy 1978; MacCrimmon et al. 1980; Cornblatt and Erlenmeyer-Kimling, in press; Erlenmeyer-Kimling et al., in press; Nuechterlein et al., in press), could lead to dysfunctions in expectancy formation. As Roth (1977) has pointed out, it is likely that task relevance and subjective probability interact, in that subjects with attentional deficits may not form accurate representations of stimulus occurrence or may not accurately perceive the probability structure of the stimulus sequence. However, when ERPs are averaged according to the sequence of stimuli that preceded the eliciting stimulus, adult schizophrenics produce sequential dependencies whose P300 amplitude and reaction time distributions are similar to those of normal controls, although the schizophrenics show overall reduced P300 amplitude and reaction time slowing relative to the normal controls (Duncan-Johnson, Roth, and Kopell, in press). Thus, the reduced P300 amplitude seen with adult schizophrenics does not seem to be due to an inaccurate perception of the probability structure of the stimulus train.

In a similar vein, it is doubtful that inattention accounts for our results since, if HR subjects were not as attentive as NC subjects, we would expect differences in performance measures between the groups. Neither mean RT and its associated variability nor any of the error rate measures of performance significantly discriminated HR from NC subjects. It is more probable that the reduced P300 amplitudes found in HR children are due to a defect in the basic cognitive mechanisms that are indexed by these late positive waveforms and may reflect dysfunctions in the neural structures responsible for their generation.

Diagnostic Specificity of P300 Reduction in Children. Children at risk for schizophrenia are not the only subjects who show reduced P300 amplitude. Both Prichep, Sutton, and Hakerem (1976) and Klorman et al. (1979) have reported reduced P300 amplitude in hyperkinetic compared with normal control subjects in a guessing paradigm (Prichep et al.) and a version of the continuous performance test (Klorman et al.). Prichep et al. (1976) reported that the hyperkinetic children's waveforms were characterized by reduced positivity which began with a negative component at 250 msec poststimulus and extended to the end of the recording epoch. This reduction in positivity appeared to reflect the marked attentional deficits which these children exhibited, as methylphenidate normalized their ERPs in both studies. It is difficult to determine whether the reduction seen in the HR children is qualitatively different from that seen in hyperkinetic children. Behavioral evidence suggestive of a qualitative difference has been presented by Nuechterlein et al. (in press), who found reduced d′ (a measure of sensitivity) in HR compared with NC subjects, whereas beta or response caution decrements characterized the hyperkinetic subjects. This performance deficit is consistent with the impulsive style of such children, a style not reported for HR subjects (e.g., Hanson, Gottesman, and Heston 1976; MacCrimmon et al. 1980; Erlenmeyer-Kimling et al., in press; Nuechterlein et al., in press). Novick and her associates (Novick, Kurtzberg, and Vaughan 1979; Novick et al. 1980) have also reported reduced P300 amplitudes in autistic relative to age-matched normal control children, whether elicited by changes in pitch or stimulus omissions (in both visual and auditory modalities). Control analyses enabled these investigators to eliminate RT variability as a cause of the reduced late positivity. The clinical symptom patterns and behavioral disturbances seen in hyperkinetic and autistic children are distinctly different and much more severe than those seen in HR children. However, the finding of reduced late positive activity in all three groups of children may reflect certain common pathophysiological mechanisms in the brain systems that underlie the generation of the cognitive ERPs.

Deviant Subjects. The fact that we restricted our analyses only to the late components (P300 and SW) and did not look at any of the earlier negative or positive waves (e.g., N100, P200, and N250) may have limited our chances of detecting outliers. Since HR children have been characterized as displaying attentional deficits, it is likely that the "vulnerable" children in the sample would exhibit a pattern of ERP response characterized by deficiencies in the earlier negativities—for example, in the N100 component or in the slow negative shift, Nd, which may underlie the N100 amplitude modulations seen in selective attention tasks (Naatanen and Michie 1979; Hansen and Hillyard 1980). However, our paradigm cannot provide evidence for deficits in selective attention, since we had no ERP index of attention to an "unattended" channel, as do the investigators using dichotic listening paradigms. It is likely, therefore, that the pattern of latency shifts and amplitude modulations of all the ERP components seen in these paradigms will have to be used to define deviant subgroups, as it is unlikely, on the basis of behavioral dysfunctions shown by HR children, that deviations in a single component will define a vulnerable individual.

From a genetic viewpoint, different models of transmission may lead to different expectations regarding whether one would expect to obtain group differences or a sharply distinct subgroup of deviant individuals. Additionally, under a multifactorial threshold model, it is possible to conceive of a situation in which some indicators may be under the control of genes having a large, major effect—suggesting that sharp outlier differences might emerge—while other indicators are themselves determined by a complex of genes such that a more generalized group difference would result. These factors aside, the small numbers of subjects in these preliminary analyses also made it less likely, on a statistical basis, for us to have detected a subgroup of significantly deviant subjects.

Conclusions

While it is currently difficult to define precisely the cause of late positive amplitude reduction in HR individuals, this pattern of ERP response, coupled with the cognitive and attentional disturbances thus far reported, is suggestive of a fundamental deficit in HR children as discussed by Garmezy (1978). The results also highlight the importance of using a paradigm that has successfully discriminated adult patients from controls, since other ERP paradigms we have used (Friedman, Vaughan, and Erlenmeyer-Kimling 1979) have not produced significant group differences. Furthermore, finding this reduction in children at risk, who have not yet become schizophrenic, suggests that reduced P300 may be a "vulnerability marker," or an enduring trait, rather than an "episode marker" indicative of a transient state (cf. Zubin and Spring 1977). Our next step will be to determine the pattern of behavioral responses and clinical status of each of the children in the HR group in order to compare these measures with our ERP indices. Our goal is to determine if a profile of measures from these different domains, which deviates from the normal, characterizes some of the HR children, as they may be the most vulnerable in the HR group.

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Effects of Stimulating Psychodynamically Relevant Unconscious Fantasies on Schizophrenic Psychopathology

by Eric Mendelsohn
and Lloyd H. Silverman

Abstract

This article reviews a series of studies investigating the relationship between various unconscious fantasies and manifest pathology in adult schizophrenics. The results support the view that the activation of specific fantasies can lead to both the exacerbation and amelioration of symptoms in schizophrenia. The theoretical and clinical implications of the experimental findings are discussed, and suggestions for further research are offered.

The purpose of this article is to present the findings from a series of studies carried out over the past 15 years investigating the effects of activating certain unconscious fantasies on the manifest pathology of adult schizophrenics. The results indicate that when stimuli designed to activate psychodynamically relevant fantasies are presented subliminally (i.e., at 4 msec exposures) to schizophrenic subjects, temporary changes in the severity of psychopathology are reliably produced. These effects do not appear after the subliminal presentation of neutral control stimuli and typically do not occur following the *supraliminal* presentation of the same psychodynamically relevant stimuli. In this communication, our research method will be described, the studies reviewed, and the findings summarized. In the concluding section, the implications of these experiments for theory and clinical practice will be discussed and suggestions for further research made.

Let us state at the outset that when we speak of unconscious fantasies affecting schizophrenic pathology, we are not taking any position on the question of etiology, nor are we claiming that psychodynamic factors are the sole or even primary contributors to symptomatic changes in adult schizophrenics. Rather, we maintain that the experimental findings to be reported indicate that the activation of different unconscious fantasies can lead to both pathology exacerbation and reduction in schizophrenia, whatever the origins of the disorder and whatever other processes may underlie symptomatic changes. These findings can thus be viewed as consistent with the formulations of clinicians (e.g., Arlow and Brenner 1964, 1969; Searles 1965) who emphasize the importance of psychodynamic factors in schizophrenia. Moreover, the experimental data allow for a specification of which fantasies are most apt to be pathogenic and ameliorative, and underscore the importance of continuing to study the role of psychodynamic factors in schizophrenia (cf. Chodoff and Carpenter 1975).

Background and Experimental Method

In the early 1960s an experimental method, referred to as "subliminal psychodynamic activation," was developed as a means of systematically studying the effects of stimulating unconscious fanta-

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sies on behavior. The method derived from the pioneering work in the field of subliminal registration carried out by Poetzl in the early 1900s and by Fisher in the 1950s (Fisher 1954, 1956). Their studies, though often not well controlled, provided support for the hypothesis that visual stimuli, registering outside of awareness, can influence subsequent behavior. Later investigations, stimulated by Fisher's work, described conditions under which subliminal effects were most likely to occur (summarized in Dixon 1971). The "subliminal psychodynamic activation method" built on these findings and attempted to use the phenomenon of subliminal registration to stimulate the kinds of unconscious fantasies[1] that psychoanalytic theory implicates in psychopathology. Soon the method was applied to the study of specific clinical psychoanalytic formulations concerning the relationship between particular unconscious fantasies and psychopathology in various clinical populations, including schizophrenics.

To date, over 50 studies have been reported (summarized in Silverman 1976, 1982) and several discussions of the implications of these findings for psychoanalytic theory have been presented (Silverman 1967, 1970, 1972, 1975, 1978*b*). Overall, the results indicate that the subliminal exposure of stimuli designed to activate psychodynamically relevant fantasies reliably affects levels of psychopathology in various clinical groups. Moreover, the results have been consistent with psychoanalytic formulations concerning the relationship between certain unconscious fantasies and psychopathology. In this report we focus on studies investigating such psychopathological changes in schizophrenics.[2]

The following is a general description of the experimental method. For the most part, inpatient and day hospital samples were used and there was often much variability within and between samples as regards chronicity, symptomatology, and severity of dysfunction. Diagnoses were determined from information provided in hospital charts and by clinical staff with at least two independent diagnostic assessments required. In one recent study (Mendelsohn 1981), more stringent criteria were employed.[3] Subjects were seen for an experimental and control session, usually on separate days, with the order of these counterbalanced. At the start of the first session, the subject was informed about the procedure and general purposes of the study, and rapport was established. He was then told about the tachistoscope, the machine used to present the subliminal stimuli. The subject was asked to describe what he observed each time he looked into the tachistoscope and was told that he would learn more about the purposes of this procedure at the conclusion of the experiment. After this introduction, a neutral "baseline" stimulus (verbal and/or pictorial) was exposed to the subject for 4 msec, followed immediately by assessments of ego pathology (usually measures of illogical, loose, or unrealistic thinking and measures of disturbed, inappropriate behavior). After these baseline data were gathered, there was a tachistoscopic exposure of the "critical" stimulus, either one designed to stimulate a psychodynamically relevant unconscious fantasy (experimental session) or one containing neutral content (control session). Following this, a reassessment of pathology using equivalent forms of the same tests used in the baseline series was made. In the second experimental session the same procedure was followed except that subjects who were shown the fantasy-related stimulus in the first session were shown a neutral stimulus in the second, and vice versa. Neither the subject nor the experimenter was ever aware of the content of the stimuli during the experiment. The scoring of the dependent measures was also carried out blindly.

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[1] An unconscious fantasy can be defined as a configuration of unconscious ideas and images containing one or more of the following components: libidinal and aggressive wishes, anxieties stimulated by these wishes, and resulting defensive operations.

[2] It should be noted that the experimental intervention, the subliminal exposure of a psychodynamically relevant stimulus, is designed to activate an unconscious fantasy *without* bringing it to consciousness. Some readers (e.g., Shapiro 1978) have assumed that the exposure of subliminal stimuli is intended to be an analog of an interpretation in psychoanalytic treatment. This is not the case insofar as an interpretation aims at making previously unconscious aims conscious, producing—among other effects—a weakening of the status of certain unconscious fantasies as motivators. Instead of viewing the activation of a psychodynamically relevant fantasy as being analogous to an interpretation, it might be more appropriate to view its impact as similar to the effects of the unanalyzed aspects of the transference to the therapist in psychoanalytic treatment. For a discussion of these points, see Silverman (1978*a*).

[3] In this study only those subjects diagnosed schizophrenic according to the criteria of Feighner et al. (1972) were included. These criteria specify the type and duration of symptoms that must be present to consider an individual schizophrenic.

In these studies the blindness of the experimenter was ensured by having him use stimulus cards that were coded on the back. These were then assigned to subjects according to a code sheet prepared by an assistant. The cards were inserted into the tachistoscope without the content being exposed. The subjects' blindness was ensured by having the stimuli exposed subliminally; this was operationally defined as a level (in terms of speed of exposure, illumination, and the qualities of the stimuli) where not only was there no recognition of any part of the stimulus, but where subjects were unable to distinguish exposures of one stimulus from those of another. That this state of affairs obtained was demonstrated in a large number of studies by administering a "discrimination task" at the end of the experiment proper. In this, as is detailed elsewhere (Silverman 1966, p. 107), subjects were asked to discriminate between exposures of one stimulus and those of another, with a monetary incentive offered to enhance motivation. Less than 10 percent of subjects (nonschizophrenics as well as schizophrenics) were able to discriminate at a rate better than chance, and the few who were (whose performance could simply be attributed to sampling error) have never accounted for the experimental effects.

The Stimulation of Aggressive Fantasies

The first group of studies we will report on are those investigating the effects of stimulating unconscious aggressive fantasies on cognitive and behavioral pathology in adult male schizophrenics.[4] It was hypothesized, based on the views of certain clinical writers (Hartmann 1953; Bak 1954) that pathology would be exacerbated following the stimulation of aggressive fantasies. As is discussed elsewhere (Silverman 1975), this formulation is at variance with the views of other clinicians who discount the role of unconscious fantasies in mediating schizophrenic psychopathology (e.g., Freeman, Cameron, and McGhie 1958; DesLauriers 1962) or those who, while acknowledging that the activation of unconscious fantasies can exacerbate pathology, maintain that it is not specifically *aggressive* fantasies that have this effect (e.g., Searles 1965). The hypothesis was subjected to repeated experimental tests, both because of the controversial nature of the clinical formulation on which it was based and because of an interest in sharpening and refining the formulation by addressing such questions as the following: (1) Which schizophrenics are most strongly affected by the stimulation of aggressive fantasies? (2) Will the stimulation of other conflictual fantasies produce similar effects? (3) Can equivalent results be obtained with supraliminal instead of subliminal stimuli? (4) What forms of pathology will most likely be adversely affected?

The studies used the basic design described above. In the "critical" portions of each experiment, the effects of a subliminal aggressive stimulus (consisting of words and/or a picture) were compared to those of a neutral control stimulus. One aggressive stimulus used was the words DESTROY MOTHER, accompanied by a drawing of a man with a knife, his teeth bared, menacing a woman. The control stimulus was the words PEOPLE ARE WALKING accompanied by a drawing of two bland-looking male figures. There were usually two dependent variables; most often measures of nonverbal pathology and disordered thinking. Disordered thinking was assessed using a number of measures, including the Rorschach, Word Association Test, and a story recall task. These instruments provided measures of loose, illogical, and unrealistic thinking, scored according to Holt's (1963) *Primary Process Scoring Manual* in the case of the Rorschach, and from manuals developed in our laboratory (available on request) for word association and story recall. Nonverbal pathology refers to any inappropriate or intrusive nonverbal behavior observed during the tests or other parts of the experimental procedure, the scoring criteria for which are also provided in a manual developed in our laboratory.

As can be seen in table 1, the subliminal presentation of aggressive stimuli produced significant increases in pathological thinking and/or nonverbal pathology when

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[4] These studies involved only male schizophrenics because the original experiments were carried out at VA facilities. Later investigators who were interested in attempting to replicate the early results similarly chose male populations.

Table 1. Studies assessing effects of aggressive stimuli on disordered thought and nonverbal pathology

Study	n	Statistical value of difference score[1] for disordered thinking	p	Statistical value of difference score[1] for nonverbal pathology	p
Forest (1977)	30	$t = 1.82$[2]	$< .04$[4]	< 1	NS
Greenberg (1977)	24	$t = -2.46$[3]	$< .05$[5]	$t = < 1$	NS
Leiter (1973)	60	$t = 1.98$	$< .05$[4]	$t = 2.90$	$< .005$[4]
Litwack et al. (1979)	30	$F = 1.41$	NS	$F = 3.50$	$< .07$[5]
Lomangino (1969)	24	$t = 2.99$	$< .005$[4]	—	—
Loveland (1977)	20	$F = 4.41$	$< .02$[5]	$t = < 1$	NS
Silverman (1966)	32	$t = 1.90$	$< .05$[4]	$t = 2.61$	$< .01$[4]
Silverman et al. (1976)	30	$t = 3.13$	$< .004$[4]	$t = 3.56$	$< .002$[4]
Silverman and Candell (1970)	30	$t = < 1$	NS	$t = 2.58$[2]	$< .01$[4]
Silverman et al. (1971)	48	$t = < 1$	NS	$t = < 1$	NS
Silverman and Spiro (1967)	40	$t = 3.18$	$< .002$[4]	$t = < 1$	NS
Silverman and Spiro (1968)	32	$t = 2.20$ $t = 1.78$	$< .02$[4] $< .04$	$t = 1.80$[6]	$< .05$[4]
Silverman et al. (1969)	52	$t = 2.45$	$< .01$[4]	$t = < 1$	NS
S.E. Silverman (1969)	48	$t = 1.86$	$< .05$[4]	$t = 4.12$	$< .005$[4]
Spiro and Silverman (1969)	32	$t = < 1$	NS	$t = 2.96$	$< .005$[4]

[1] The t values are based on the difference between change scores between the baseline and critical portions of experimental and control sessions. Net pathology increases were, for the most part, based on increases in pathology after the aggressive stimuli rather than decreases in pathology after the critical control stimuli.

[2] Used "earlier" and "later" ratings of pathology and obtained significance only on "later" ratings.

[3] Pathology *decrease*.

[4] One-tailed test.

[5] Two-tailed test.

[6] Not reported in original article.

compared to the effects of a neutral control stimulus in 13 of the 15 studies conducted using this paradigm.[5] Studies in which such results were not obtained will be briefly discussed later in this section.

Let us now summarize the findings with respect to the questions posed above:

1. Which schizophrenics are most strongly affected by the stimulation of aggressive fantasies? Chronicity has been found to be positively correlated with susceptibility to subliminal aggressive stimuli; that is, the longer a schizophrenic has been hospitalized, the greater his tendency to demonstrate an increase in pathology following the aggressive condition (Silverman 1971; Loveland 1977). On the other hand, no consistent differences have been found between paranoid and nonparanoid subjects (Silverman and Spiro 1968; Lomangino 1969; S. E. Silverman 1970; Forest-Letourneau 1977). Further, Litwack, Wiedemann, and Yager (1979) found that when their subjects were dichotomized into groups with (a) high and low baseline pathology scores and (b) strong and weak defenses against aggression (as determined by their conscious associations to the aggressive stimuli after the experiment proper had been completed), those with high baseline scores and weak defenses carried the experimental effects. Coupling these findings with the results on chronicity noted above, it would appear that schizophrenics who are most susceptible to the activation of unconscious aggressive fantasies are those with the fewest adaptive resources, psychologically speaking.

2. Will other conflictual stimuli produce similar effects? Attempts have been made to determine whether it is *only* aggressive fantasies which, when stirred up, lead to increases in pathology in schizophrenics. In four studies (Silverman and Silverman 1967; Silverman et al. 1969; S. E. Silverman 1970; Silverman, Bronstein, and Mendelsohn 1976), other conflictual fantasy-related stimuli were tested along with aggressive stimuli, the former including stimuli with incestuous, exhibitionistic, and homosexual content. The results were that while the other fantasy-related stimuli sometimes affected measures of cognitive efficiency and nonverbal pathology, only the aggressive stimuli produced increases in thought disorder, a symptom that may be more specific to schizophrenia.

Also related to the question of the specificity of unconscious fantasies was a finding of Lomangino (1969). He examined the effects on disordered thinking in schizophrenics of two oral-aggressive stimuli and two aggressive stimuli without an oral element. Only the former produced a significant change on his dependent measures. This then led to an examination (Silverman 1975) of all the stimuli that produced effects in the studies reported in table 1; of the nine different aggressive stimuli that have been used, all were found to have an oral element (e.g., a lion roaring).

The question of the specificity of the relationships between unconscious fantasies and symptomatic changes was examined from another vantage point as well. The question asked was whether the same stimuli that produced increases in schizophrenic psychopathology would exacerbate symptomatology in other clinical groups. In one of the studies cited above (Silverman et al. 1976) it was found that a sample of schizophrenics showed increases in thought disorder and nonverbal pathology following exposure of the stimulus DESTROY MOTHER, but not after a stimulus designed to activate an incestuous fantasy. Conversely, in a sample of male homosexuals, the incestuous stimulus produced an intensification of homosexual feelings and anxiety while DESTROY MOTHER produced no change on either measure. In this same study DESTROY MOTHER did produce a pathology increase in a sample of depressed women, while a stimulus with anal content did not. On the basis of additional data from this and other studies, it was concluded that pathology intensifications can only be reliably produced by a subliminal stimulus whose content is relevant for the clinical group being studied. Consistent with predictions derived from psychoanalytic formulations, the oral aggressive stimulus produced exacerbations of pathology in depressives as well as schizophrenics.

3. Can equivalent results be obtained with supraliminal aggressive stimuli? By and large, the answer has been "no." Whereas

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[5] From the point of view of ethical considerations, it should be pointed out that experimental effects have typically proved to be mild, with the degree of pathology rapidly reverting to its baseline level. For a full discussion of ethical issues involved in subliminal psychodynamic activation research, see Silverman (1977).

experimental effects regularly were obtained with subliminal aggressive stimuli, supraliminal exposure to the same stimuli only rarely produced effects. As has been discussed elsewhere (Silverman 1972), this can be attributed to the fact that the possibility of mastering disturbing mental content is considerably greater when a person is aware of what in his environment is eliciting it. In three studies with schizophrenics (Silverman and Spiro 1968; Lomangino 1969; Silverman and Candell 1970), a significant increase in pathology occurred after the subliminal presentation of an aggressive stimulus, while no effect was noted when the same stimulus was exposed supraliminally.[6] In the studies in which supraliminal presentations of aggressive stimuli did produce increments in psychopathology, the results occurred in the context of modifications of the usual procedure. Thus in the study by Silverman and Spiro (1968), one of those just cited in which a supraliminal aggressive condition did *not* lead to an intensification in pathology, a second supraliminal aggressive condition did result in such intensification. However, for this latter condition, in contrast to the first, subjects were required to describe the aggressive picture that they saw. As is detailed elsewhere (Silverman 1972), it was hypothesized that this interfered with the ability to master, through conscious fantasy expression, the aggressive ideas and feelings stirred up by the stimulus. In another study not listed in table 1 (Moriarty 1968), supraliminal aggressive stimuli produced pathological changes on some measures of cognitive efficiency. However, the author did not include tests of disordered thought and nonverbal pathology, the measures which typically carry the subliminal effect.

4. What forms of pathology will most likely be adversely affected? In the studies summarized in table 1, a variety of different dependent variables were employed. It was found that various measures of disordered thought, specifically, thinking that is loose, illogical, and disorganized, and the "nonverbal pathology" measure (i.e., behaviors that are inappropriate in the experimental setting or are otherwise disturbed) were most reliably affected by subliminal aggressive stimuli. Measures of "cognitive efficiency," usually assessments of the accuracy of a story recall or performance on Wechsler Adult Intelligence Scale (WAIS) subtests, only occasionally produced an effect (Silverman and Silverman 1967; Silverman and Spiro 1967, 1968; Moriarty 1968; Lomangino 1969; Spiro and Silverman 1969; S.E. Silverman 1970).

After the foregoing review of the major experimental findings, it is reasonable to consider the question of their reliability. There were two studies, one from our laboratory (Silverman et al. 1971) and one independent investigation (Greenberg 1977), in which subliminal aggressive stimulation did not intensify pathology in schizophrenic subjects. A post hoc explanation can be offered for each of these nonreplications,[7] but we think the more important point is that 13 of 15 positive results compares favorably to other research on schizophrenia and establishes the finding under consideration here as reliable. However, it should be noted that this reliability only extends to the *groups* of schizophrenics tested; there were always a number of participants in each sample who did not demonstrate the experimental effect. Thus, it must be said that the formulation that we studied, namely, that the activation of unconscious aggressive fantasies produces intensifications of psychopathology, has been demonstrated for some schizophrenics, but not for others. The findings on "adaptive resources" noted earlier offer the best lead, as of now, as to what differentially characterizes the two groups.

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[6] This finding has received added support from three studies of nonschizophrenics (Silverman and Goldweber 1966; Rutstein and Goldberger 1973; Silverman et al. 1973) where the subliminal presentation of a wish-related stimulus produced a change in psychopathology while the supraliminal presentation of the same stimulus did not.

[7] In the study of Silverman et al. (1971), the absence of any findings after the aggressive condition was attributed in the original report to a procedural difference distinguishing this experiment from the others summarized in table 1. In Greenberg's (1977) investigation, on the other hand, as can be observed in table 1, there was a significant *reduction* in pathology following the subliminal aggressive stimulus, a paradoxical finding for which the author could offer no explanation. Greenberg kindly made available to the second author of the current article Rorschach responses (used as a dependent measure) that he had collected from his subjects. An examination of these suggested that the pathology reduction may have been a function of a general constriction that followed the aggressive condition. Perhaps then, Greenberg's subjects were of the more resourceful kind described earlier and were able to maximize their adaptive efforts in the face of threat, leading to fewer pathological expressions, but at the expense of ideational freedom. Obviously, this interpretation can be considered as no more than a speculation at present.

Summary

The "subliminal psychodynamic activation" method has enabled us to investigate and refine an important clinical psychoanalytic formulation concerning unconscious fantasies and intensification of pathology in schizophrenia. The results indicate that the activation of oral-aggressive fantasies produces (temporary) increases in certain types of pathology in groups of male schizophrenic subjects. Further, it has been found that libidinal stimuli may affect cognitive efficiency and/or nonverbal pathology, but only oral-aggressive stimuli produce increases in disordered thinking. That these results tend not to hold when experimental stimuli are visible to subjects is consistent with the view that once a stimulus that activates disturbing mental content reaches awareness, its status as a motivator may be diminished.

The Stimulation of Oneness Fantasies

The second series of studies we will review investigated the hypothesis that the activation of what has been termed a fantasy of "symbiotic-like gratification" (Silverman, Lachmann, and Milich, in press) may lead to clinical improvement in schizophrenia. This (unconscious) fantasy can be defined as one in which certain representations (or aspects) of the self are merged with representations of an other. This "other" may be a currently significant figure that is unconsciously associated with the "good mother of early childhood." This hypothesis is grounded in psychoanalytic developmental psychology (Mahler 1968; Mahler, Pine, and Bergman 1975) and is supported by the reports of a number of clinicians (Harris 1974; Limentani 1956; Little 1960; Searles 1965) that schizophrenics often show improvement during psychotherapy after they give evidence of merging representations of themselves with representations of the therapist, the latter unconsciously perceived as the good mother of early childhood. This hypothesis is also a controversial one and runs counter to the suppositions of another group of clinicians (Freeman, Cameron, and McGhie 1958, 1966; DesLauriers 1962) who maintain that the merging proclivities of schizophrenics are the result of an unmotivated boundary disturbance. At least implicit in their formulation is the prediction that the gratification of wishes for oneness will prove antitherapeutic. Because these divergent hypotheses are of both theoretical and clinical importance, and because controversy about them is very much alive among clinicians, we attempted to examine them experimentally. The studies we will review assessed the effects of stimulating a fantasy of oneness gratification on disordered thinking and nonverbal pathology in adult male schizophrenic subjects.

The experimental procedure was identical to the one described earlier, except that the crucial experimental stimulus was the phrase MOMMY AND I ARE ONE (with the assumption that the word "mommy" refers to the "good mother of early childhood") sometimes presented by itself and sometimes accompanied by a line drawing of a man and a woman partially joined together at the shoulders like Siamese twins. The prediction was that this stimulus would have a pathology-*reducing* effect when exposed subliminally to adult schizophrenics. As in many earlier studies, the control stimulus was usually PEOPLE ARE WALKING, either presented alone or together with a congruent picture in the studies where a picture accompanied MOMMY AND I ARE ONE. The dependent variables again usually were disordered thinking and nonverbal pathology.

The results of both our own studies and the replications by others are summarized in table 2. As can be seen, the hypothesis that the MOMMY AND I ARE ONE stimulus would prove ameliorative was borne out in 10 of 11 studies. Again, it should be noted that experimental effects in this group of studies were mild and short-lived.[8,9] In these investiga-

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[8] The one nonreplication was the study by Loveland (1977) cited in table 1 as one of those investigations that replicated the finding that subliminal *aggressive* stimulation intensifies psychopathology. With regard to her nonreplication of the MOMMY AND I ARE ONE effect, Loveland pointed out that a variation occurred in the normal selection procedure for subjects, which may have prevented a replication. Moreover, as is discussed elsewhere (Silverman, Lachmann, and Milich, in press), the

tions, the following additional questions were addressed: (1) Is the schizophrenic's level of differentiation relevant to whether the gratification of symbiotic-like wishes will prove ameliorative? (2) How specific is the fantasy that leads to pathology reduction in schizophrenics? We will briefly take up these two questions in turn.

1. Is the schizophrenic's level of differentiation relevant to whether the gratification of symbiotic-like wishes will prove ameliorative? In the original study, the stimulus MOMMY AND I ARE ONE produced a reduction in thought disorder that approached, but did not reach, significance (Silverman et al. 1969). However, a post hoc analysis was performed on the data and an interesting finding emerged. For a different purpose, each subject had been administered what came to be referred to as a "self-mother differentiation scale." This measure required the subject to rate himself for a series of 20 descriptive adjectives according to a 6-point scale and then to rate the picture of a neutral-looking older woman of the same race as he, for the same adjectives. The woman was intended as a mother figure, and since little information could justifiably be inferred from the photo, the degree to which the ratings of the woman were similar to the self-ratings was taken as a measure of self-mother differentiation. In the initial study, when the differences between self- and mother-figure ratings were totalled, it was found that those subjects who scored as "relatively differentiated" (i.e., those in the upper half of the distribution when the scores were subjected to a median split) showed a significant reduction in disordered thinking following exposure to the oneness stimulus, while the "relatively undifferentiated" half of the sample did not. Silverman et al. (1969) then subjected this post hoc finding to a more stringent test by selecting a group of relatively differentiated subjects on this same scale (using the median split cutoff score from the original study as the criterion) and exposing them to the MOMMY AND I ARE ONE and control stimuli. The result was a significant reduction on the disordered thinking measure for the oneness condition.

Leiter (1973) attempted to replicate this finding and used samples of both relatively differentiated and undifferentiated schizophrenics. He found that the former showed significant reduction in disordered thinking following the oneness stimulus, while the undifferentiated subjects showed a significant pathology *increase* on the same measure. T. Spiro (1975) and Fribourg (1981) found no change for undifferentiated subjects, while replicating the pathology-reducing effect for differentiated schizophrenics. In all the other studies listed in table 2, only samples of relatively differentiated schizophrenics were used, and in all but one of these the pathology-reducing effect of the oneness stimulus was demonstrated.[10] Thus, the self-mother differentiation scale has proven to be a reliable predictor of response to the oneness stimulus.

In light of the differences that have been found in the responses of relatively undifferentiated and differentiated schizophrenics to the experimental stimulus, and bearing in mind the views of clinicians who consider the gratification of symbiotic-like wishes as antitherapeutic, the following formulation was proposed. We reasoned that the MOMMY AND I ARE ONE stimulus produced no improvement (and in one study, a pathology increase) in the undifferentiated subjects because such schizophrenics tend to experience the further merging of self-

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word "mama" rather than "mommy" is the standard term used by children to refer to their mothers in the South where Loveland's study was conducted. (All of the other studies listed in table 2 were carried out in the North.) Thus, it was posited that the word "mommy" did not have the same connotations for her subjects that it had for subjects in the other studies—that of the good mother of early childhood (Silverman, Lachmann, and Milich, in press). Support for this interpretation was furnished by the finding that in the investigations carried out in the North, the MOMMY AND I ARE ONE stimulus, although equally affecting black and white subjects, did not affect Hispanic subjects who were raised in homes where English was not the language spoken during their infancy.

[9] The results of one further study lend weight to the conclusion that pathology level can be affected by whether or not a schizophrenic fantasizes himself as experiencing symbiotic-like gratification. Litwack, Wiedemann, and Yager (1979) found that the stimulus I AM LOSING MOMMY, which can be viewed as activating a fantasy of *frustrated* wishes for oneness with mother, produced a significant *increase* in pathology.

[10] Again it should be noted that experimental effects in this group of studies have been mild and short-lived.

Table 2. Studies assessing effects of oneness stimuli

Study	*n*	*t* value of difference score[1] for disordered thinking	*p*	*t* value of difference score[1] for nonverbal pathology	*p*
Bronstein (1976)	30	2.93	< .01[2]	1	NS
Fribourg (1979)	20	2.23	< .04[2]	2.52	< .03[2]
Kaplan (1976)	32	3.67	< .001[2]	1.86	< .1[2]
Kaye (1975)	32	.409	NS	1.92	< .05[3]
Leiter (1973)	30	1.91[4]	< .05[3]	1.70	< .1[3]
Loveland (1977)	20	1	NS	1	NS
Mendelsohn (1981)	54	1	NS	2.13	< .025[3]
T. Spiro (1975)	20	2.57	< .025[2]	1	NS
Silverman and Candell (1970)	30	1.96	< .03[3]	1	NS
Silverman et al. (1971)	48	1	NS	2.40[4]	< .02[3]
Silverman et. al. (1969)	18[5]	1.78	< .05[3]	—	—

[1] The *t* values are based on the difference between change scores between baseline and critical portions of experimental and control sessions. Net pathology decreases were, for the most part, based on decreases in pathology after the oneness stimulus rather than increases in pathology after the critical control stimulus.

[2] Two-tailed test.

[3] One-tailed test.

[4] Gave "earlier" and "later" dv's and obtained significance only on "earlier."

[5] Initially a mixed group of 20 "differentiated" and "undifferentiated" subjects were studied. For this group there was a trend toward pathology reduction on the pathological thinking measure ($t = 1.63$, $p = .06$, one-tailed). When post hoc analyses indicated that level of differentiation was a crucial variable affecting responses to MOMMY AND I ARE ONE, a second sample of 18 "differentiated" subjects was run.

and object-representations that the stimulus activates as threatening their sense of self. Experimental data in support of this view were obtained in a study in which a new stimulus—the message I AM MOMMY—produced significant *increases* in pathology, even among relatively differentiated schizophrenics (Silverman 1970). This message was seen as activating a merging fantasy in which there is *no* distinction between self and mother. In light of these results we concluded that whether or not activating a fantasy of symbiotic-like gratification will prove ameliorative for a schizophrenic depends on the degree to which sense of self can simultaneously be preserved.

2. How specific is the fantasy that leads to pathology reduction in schizophrenia? Kaye (1975) varied the verbal stimulus to see whether the fantasy of oneness, in order to be ameliorative, had to have MOMMY as its object. To this end he compared MOMMY AND I ARE ONE with DADDY AND I ARE ONE and MY GIRL AND I ARE ONE. He found that the "mommy" and "my girl" messages produced improvement while "daddy" did not. One plausible interpretation of this finding is that for the oneness fantasy to be therapeutic, it must have as its object a (benign) maternal representation rather than a representation of any significant other.

Kaye's study, like all of those under discussion, involved male schizophrenics. Cohen (1977) for the first time used the experimental paradigm to study female schizophrenics. While the MOMMY AND I ARE ONE stimulus produced no effect, Cohen found that DADDY AND I ARE ONE reduced pathology for this group. In a very recent study (Jackson 1981), this result was replicated, as was the finding of pathology reduction with the MOMMY AND I ARE ONE stimulus with male schizophrenics. These findings, along with Kaye's (1975), suggest that the most desirable object of a oneness fantasy can vary among schizophrenics. The differences in responses between men and women may be accounted for by Lidz's (1973) observation that female schizophrenics often turn from mother to father as the object of symbiotic-like longings. Thus, for some subjects, words like "daddy" or even "my girl" may better connote the fantasized good mother of early childhood than does "mommy." Further research in this area is clearly needed.

In another group of studies in which the MOMMY AND I ARE ONE stimulus was analyzed, several investigators looked at the element of "oneness" to determine whether this was necessary to produce the experimental effect. Bronstein (1976) contrasted MOMMY AND I ARE ONE with stimuli designed to activate different internalization fantasies. Using Schafer's (1968) definitions of internalization, he compared the stimuli MOMMY IS INSIDE ME (introjection), MOMMY AND I ARE THE SAME (sameness identification), MOMMY AND I ARE ALIKE (likeness identification), and MOMMY AND I ARE ONE (oneness identification) with a neutral control stimulus. Bronstein found that while the "oneness stimulus" produced the same pathology reduction reported in earlier studies, none of the other internalization messages had this effect.

In another study, Kaplan (1976) tried to determine if, in addition to the oneness fantasy, other kinds of gratifying or reassuring fantasies involving "mommy" were ameliorative. To this end she presented MOMMY AND I ARE ONE, the neutral control stimulus, and MOMMY IS ALWAYS WITH ME (reassurance against separation anxiety), MOMMY FEEDS ME WELL (oral gratification), and I CANNOT HURT MOMMY (reassurance against the harmful effects of aggressive wishes). Again, only the oneness stimulus produced a significant reduction of pathology.

On the other hand, Fribourg (1981) found that the stimulus MOMMY GIVES ME EVERYTHING led to improvement on the nonverbal pathology measure but not on the measure of disordered thought, whereas MOMMY ARE I ARE ONE produced improvement on both measures. She concluded (taking into account the findings of Bronstein and Kaplan discussed above, as well as her own) that it may be only the oneness fantasy that is ameliorative for thought disorder, a symptom that may have more specificity for schizophrenia than nonverbal pathology. This conclusion is consistent with the results of a recent study by Silbert (1982). He found that while the MOMMY AND I ARE ONE stimulus reduced thought disorder, the other stimuli he was investigating—MOMMY AND I ARE ALL, I MAKE MOMMY WHOLE, and MOMMY HOLDS ME SAFELY, while affecting other measures, had no effect on disordered thought.

One other study warrants description here. Mendelsohn (1981) tested the effects of three stimuli on relatively differentiated male schizophrenics: MOMMY AND I ARE ONE, MOMMY AND I ARE TWO, and a control. Each of the first two stimuli was accompanied by a picture of a man and a woman—in the former condition, joined at the shoulders, while in the latter, simply next to each other. *Both* MOMMY stimuli led to reduced pathology, and interestingly, the TWO stimulus produced a significantly greater effect than the ONE stimulus.

Does this finding contradict the conclusion that it is specifically a fantasy of oneness that is most ameliorative for relatively differentiated schizophrenics? We do not think so; rather, we think this finding adds to our understanding of the therapeutic effects of symbiotic-like fantasies. When associations were obtained to both MOMMY stimuli (i.e., both the messages and the accompanying pictures) from a number of the subjects after the experiment was completed, it was found that many of the associations to MOMMY AND I ARE TWO had much in common with those to MOMMY AND I ARE ONE. That is, the TWO stimulus, rather than eliciting associations pertaining to the frustration of symbiotic-like longings, as it had been thought beforehand it might, instead stimulated ideas about togetherness and even a figurative oneness. At the same time subjects often gave associations suggesting they felt protection against identity loss.[11] From this it would seem that the MOMMY AND I ARE TWO stimulus activated a fantasy involving oneness elements, but one which allowed for greater differentiation from the mothering figure. That is, in keeping with the point made earlier about oneness fantasies being potentially threatening as well as gratifying, the TWO stimulus (at least when accompanied by the picture that was described) seemingly had the effect of providing a symbiotic-like gratification while avoiding a mobilization of threat to sense of self. Further study of this possibility is being planned.

One final note about the issue of specificity. Earlier we presented findings indicating that stimuli such as DESTROY MOTHER did not produce pathology intensification in *all* clinical groups, but only in groups such as schizophrenics and depressives in which a connection is postulated between oral aggressive fantasies and psychopathology. A different situation has been found to obtain with the oneness stimulus. Results from many studies (summarized in Silverman 1978*b*; Silverman, Lachmann, and Milich, in press) indicated that the activation of symbiotic-like fantasies (especially when the experimental stimuli have been exposed repeatedly over a period of several weeks) produced pathology reduction in several different clinical groups and generally enhanced adaptation in a number of nonclinical samples. See Silverman, Lachmann, and Milich (in press) for further discussion of these findings.

Summary

The results presented in this section indicate that the stimulation of a fantasy of symbiotic-like gratification reliably produces temporary symptomatic improvement in samples of "differentiated" adult male schizophrenics. Earlier we reported that increases in pathology were obtained in schizophrenics after exposure to a variety of fantasy-related stimuli, but only oral aggressive stimuli produced increases in thought disorder. Analogously, whereas recent data suggest that several gratifying fantasies may produce ameliorative effects, only stimuli that activate fantasies of symbiotic-like gratification have affected disordered thinking.[12] The results also suggest that the ameliorative effect of the oneness fantasy is conditional because it may have disturbing as well as therapeutic connotations. Several studies designed to identify the conditions under which the oneness fantasy is ameliorative and to determine, specifically, what therapeutic elements are associated with it have yielded data indicating that it may be ameliorative under some circumstances and disturbing under others. The crucial variables seem to be the level of differentiation of the schizophrenic and the degree to which self- and mother-representations are merged in the fantasy. Further work to identify critical therapeutic factors is clearly needed.

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[11] A related finding, and one very relevant to this discussion, recently emerged from a subliminal psychodynamic activation study involving nonschizophrenics. Dauber (1980) found that MOMMY AND I ARE TWO, accompanied by the same picture that Mendelsohn used, was ameliorative for a group of depressed college women. The more important finding from this study, however, was that when Dauber collected associations to the stimulus after the experiment proper had been completed, he was able to divide his sample into subjects whose associations referred to themes of separation and alienation on the one hand and themes of togetherness and figurative oneness on the other. It was only the latter subgroup that carried the experimental effects.

[12] See Silverman (1970) for a rationale based on psychoanalytic theory to account for the link between thought disorder and activated oneness fantasies.

Discussion

In this article we have summarized a series of experiments demonstrating that certain behavioral and cognitive disturbances typically manifested by schizophrenics can be reliably—if only temporarily—modified via the stimulation of psychodynamically relevant unconscious fantasies. We believe these results have theoretical and clinical importance. In terms of theory these experiments are relevant to the debate that has taken place in recent years among members of the mental health community (Silverman 1975) as to what role, if any, psychodynamic variables play in affecting the primary psychopathological manifestations of schizophrenia. We believe the data are supportive of the formulations of those who maintain that schizophrenic symptoms are at least partially mediated by unconscious conflict (Arlow and Brenner 1964, 1969; Searles 1965). In some instances the results are counter to the formulations of other writers who maintain that while schizophrenics, like all people, have unconscious conflicts, these do not, as a rule, bear significantly on their schizophrenic symptoms (DesLauriers 1962; Holzman 1975; Wexler 1975). While the experimental data do not, by any means, preclude the presence of preexisting or concurrent constitutional deficits, they are consistently supportive of particular psychodynamic formulations. One way of integrating these findings with current knowledge about etiology would be to say that for reasons that may relate to the existence of innate deficits, or adverse experiences early in life, or both, schizophrenics are characterized by sensitivities to the stimulation of both aggressive and symbiotic-like fantasies. It remains the task of further experimental study to determine what subject and stimulus variables are most relevant to producing behavioral changes.

The studies that have been reported enable us to specify the kinds of unconscious fantasies that mediate symptomatic changes in schizophrenics. Two findings would appear to be of particular importance. As noted earlier, whereas the activation of libidinal fantasies can *intensify* some kinds of pathology in schizophrenics, with regard to the specific symptom of thought disorder, only aggressive fantasies—and more specifically, oral-aggressive fantasies—produce pathology increases. And second, whereas the activation of certain unconscious fantasies involving gratification by the "good mother of early childhood" can *ameliorate* schizophrenic pathology, again with regard to the specific symptom of thought disorder, only fantasies related to oneness are mutative. Further, with regard to oneness fantasies, it appears that these will be ameliorative only when their presence does not threaten boundary loss. Thus, if either a schizophrenic is relatively undifferentiated from his mother, or if the oneness fantasy involves too many self-representations that are merged with mother representations, the consequences will not be positive.

Turning from theory to treatment, the data from the experiments on the oneness fantasy can be seen as having bearing on a controversy that has long existed in the clinical community. There has been one group of therapists (Sechehaye 1951; Limentani 1956; Little 1960; Searles 1965; Harris 1974) who see as a central task in the treatment of schizophrenics the therapist helping the patient to obtain in his relationship with him safe symbiotic-like gratifications. On the other hand, there has been a group (DesLauriers 1962; Freeman, Cameron, and McGhie 1958; Lidz 1973) who see as the central task the strengthening of "self-boundaries." Whereas many of these clinicians (particularly those in the second group) seem to view these aims as antithetical, the findings that have been reported here suggest that this is not the case. That is, the many positive results with the MOMMY AND I ARE ONE stimulus indicate that oneness fantasies can indeed be ameliorative for schizophrenics; on the other hand, the results relating these findings to differentiation level, the pathology-intensifying effects found for I AM MOMMY, and the pathology-reducing effects found for MOMMY AND I ARE TWO indicate that the strengthening of self-boundaries also has a place in treatment. Thus the experimental data indicate there is validity to the views of both groups of clinicians cited above. As has been proposed in detail elsewhere (Silverman, Lachmann, and Milich, in press), perhaps the therapeutic aims of fostering oneness experiences and enhancing sense of self can be reconciled by concluding that to the extent that boundaries are strengthened, the schizophrenic will feel more comfortable allowing himself oneness fantasies with their ameliorative consequences.

There is one other treatment implication of the studies involving subliminal symbiotic-like stimuli that we would like to propose tentatively. It relates to using the tachistoscopic intervention for activating oneness fantasies as a treatment aid. As we noted earlier, the symptomatic changes produced by the MOMMY AND I ARE ONE stimulus in the laboratory studies that have been described have been of very brief duration. However, two treatment studies (Milich 1975; Silverman et al. 1975) with schizophrenic subjects also have been carried out. The design of these was that each subject was seen for several sessions a week for 6 weeks. Subjects received regular "doses" of either the subliminal symbiotic-like stimulus or a subliminal control stimulus. These were administered in combination with other experimental therapeutic interventions such as a self-focusing procedure (designed to strengthen self-boundaries) and a guided fantasy technique. In one study (Silverman et al. 1975) the experimental group, when compared with the controls, showed significantly greater improvement on two of seven measures of "ego pathology" after the 6-week treatment period and produced a nearly significant difference in the number of rehospitalizations during a 9-month followup period. In the second study (Milich 1975) there was a replication of the initial (6-week) pathology reduction, though no significant group differences were found on followup after 2 months.

These results are admittedly weak. However, when they are considered in conjunction with five recent studies (Bornstein 1980; Bryant-Tuckett 1980; Linehan and O'Toole 1982; Parker 1982; Ariam and Siller, in press) demonstrating that, with nonschizophrenic populations, subliminal stimulation of oneness fantasies has produced powerful therapeutic effects,[13] they suggest the possibility that the further development of this intervention may allow it to be of substantive value in the treatment of certain schizophrenics.

In closing, we would like to note the areas in which further research on subliminal stimulation of oneness fantasies with schizophrenics is most needed: (1) the investigation of subject variables affecting responses, such as subtype of schizophrenia, stage of illness, differentiation level, family history, the associations of subjects to the MOMMY AND I ARE ONE stimulus, and hemisphericity (a variable which may affect susceptibility to subliminal psychodynamic stimuli in general); (2) the further study of the specificity of the oneness stimulus, including an attempt to replicate Mendelsohn's (1981) finding of pathology reduction with the "twoness" stimulus; and (3) investigations of whether increased dosage and variations in the wording of the oneness stimulus will increase the therapeutic impact of the intervention.[14]

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[13] For a comprehensive report and discussion of studies in which subliminal symbiotic stimulation has been used as a treatment aid, see Silverman, Lachmann, and Milich (in press).

[14] Currently, a hospital study is being conducted (Cooper, in progress) in which four groups of schizophrenics are being compared. One is receiving standard dosages of neuroleptic medications and the other three have been temporarily withdrawn from medication and are instead receiving subliminal stimulation several times a day. For one of these groups a neutral (control) stimulus is being exposed, while for the other two, the stimuli are MOMMY AND I ARE ONE and MOMMY AND I ARE TWO, respectively. This is the first instance in which the "effect size" of this intervention is being compared to that of a known therapeutic agent.

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First Person Account: Maintaining Mental Health in a Turbulent World

by Joan F. Houghton

The article and the poems that follow are part of the *Schizophrenia Bulletin*'s ongoing *First Person Accounts* series. We hope that mental health professionals—the *Bulletin*'s primary audience—will take this opportunity to learn about the issues and difficulties confronted by consumers of mental health care. In addition, we hope that these accounts will give patients and families a better sense of not being alone in confronting the problems that can be anticipated by persons with serious emotional difficulties. Although there are a number of books and articles describing the personal experiences of patients and families with mental disorder, we believe there is a continuing need for experiences to be shared among mental health professionals, families, and current and former patients.

We welcome other contributions from patients, ex-patients, or family members. Our major editorial requirement is that such contributions be clearly written and organized and that a novel or unique aspect of schizophrenia be described, with special emphasis on points that will be important for professionals. Clinicians who see articulate patients, with experiences they believe should be shared, might encourage these patients to submit their articles to *First Person Accounts,* Center for Studies of Schizophrenia, NIMH, 5600 Fishers Lane, Rm. 10–95, Rockville, MD 20857.

In memory of Ina Jean,
a friend, whose laughter continues
to ring in our hearts and whose hope
was lost in the struggle to survive
in a turbulent world.

My mother and I sat next to each other in the waiting room while my father investigated admission procedures. A young man was seated near us. Perspiration dripped across his brow and down his cheeks. In silence I took a tissue from my purse, moved close to him, and gently wiped the moisture from his face. I reassured him that everything would be fine.

Soon my father rejoined us. We went together to a small room where I met Kay, the psychiatric social worker assigned to my case, and a psychiatrist (whose name I don't recall). We talked a few minutes. I was presented with a piece of paper and instructed to sign my name. Obediently, I wrote "Saint Joan" on the paper, not realizing that I was voluntarily admitting myself to a state mental hospital.

This is a preview of a tragedy in my life which I find difficult to remember 5 years later. The difficulty is a function of the fact that my reality is your reality—that I, like you, struggle to cope and survive each day in a turbulent world. The difference between us is an experience which has changed every aspect of my life. It is the changes and not the experience that I want so much to share with you.

In order to replace mental illness

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with mental health, considerable learning and relearning had to occur. To survive and cope, I had to begin my life over again, to adopt a new, healthier style of living. By learning more about myself, my limits, and weaknesses and strengths, and by making changes in my way of life, I have been able to maintain my health and prevent a recurrence of mental illness. My first psychotic episode and the hospitalization experience set the conditions for these changes to happen cataclysmically.

At the time of my hospitalization I had both a sense of death and a rebirth about me. My first psychotic episode appeared as a private mental exorcism, ending with the honor of sainthood and the gifts of hope and faith. Fortunately, this sense of power became a source of tremendous strength during my recovery and sustains me even today.

Then, and in my memory, my hospitalization was an entombment; the medications were an embalmment. I walked among the living dead. It was not so much cruel as morbid and morose. It lasted 5 eternal weeks.

In the real world the sense of death remained for years, until I stopped ingesting medications. The transformation was extraordinary: My face was no longer swollen; extra pounds began to melt away; my hair grew thicker and more manageable; my movements were no longer mechanical and forced; my energy level increased. I had a tremendous sense of rebirth.

To maintain a sense of well-being, I have had to change my lifestyle and my priorities. My illness taught me (the hard way) the importance of meaningful work, good patterns of rest and sleep, exercise, diet, and self-discipline. Once freed from the regulating shackles of medications, I had to substitute their positive effects—a reasonable routine, a slower pace, and a calm atmosphere.

I began my new life by setting up a schedule for myself, by providing a structure for everyday living. I put the schedule for "the ideal day" and "the ideal week" in a small black notebook which I kept in my purse or briefcase. The notebook also stored a calendar and addresses and phone numbers, and a running list of tasks to be accomplished. It reminded me of what was important.

Although I no longer carry the notebook, parts of it remain recorded in my thoughts. Even now, I schedule in "down time" at the end of the day—about 30 minutes to an hour of quiet before bedtime to read, write in my diary, lounge in a tub of hot water. Because television, phone calls, rock music, exercise, or other mentally or physically stimulating activities can disturb my sleep patterns, I avoid them whenever possible before bedtime.

Although my daily eating habits have not changed that drastically, I give careful attention to dieting. I never eliminate a food group—balanced meals are essential to good health, mental and physical. I minimize consumption of foods which have proved harmful to me—sugar, coffee, and other stimulants. For me, sugar intake is a critical indicator of my general health and well-being. When I crave sweets, especially sugar candies, I am typically very tired and working under stress. This is a sign to take a day off from work and rest. Coffee, cokes, and other caffeinated beverages are rarely consumed because they generate nervous energy. I reluctantly take medications, even aspirin, unless I am physically very ill or in great pain. Occasionally, if I have trouble sleeping, I drink a glass of wine. When I'm feeling "down," I give in to my one dietary weakness: potato chips. (Food frustrations can be very harmful, in my opinion.)

Exercise and physical activity not only strengthen the body but serve as an emotional safety valve. A tennis racket, a softball bat, or a golf club is an excellent means for displacing anger. Running is often effective in alleviating depression. Dancing and swimming can be equally beneficial for lethargy and withdrawn personalities.

From my perspective, mental illness is often negative energy turned inward; exercise provides a healthy release for this energy. Physical activity serves in a paradoxical way to build and exhaust the body. A well-balanced exercise program is as essential as a well-balanced meal—too much, too little, or the wrong types of exercise can be as detrimental as too much, too little, or the wrong types of food.

My own exercise program is varied because I like to participate in most sports. Because some activities, such as tennis, frustrate me, I avoid matches which are too competitive. Since my back and knees cry out in pain when I run, climb steep mountains, or exercise too long, I minimize these activities. A bike ride or hike in the woods can be very emotionally and mentally rejuvenating.

The second major area of my life in which I learned to change involved my mental processes and intellectual development.

Psychotic episodes have the effect of "playing" mental messages on 78+ and frequently switching stations. Disorganized thoughts are often best managed in organized environments. Impulsive obsessive-compulsive behaviors have been a critical indicator that my mental world is not well ordered. I have learned to manage this by a process I call "mental purging."

If I have had a particularly busy day, if someone has upset me, or if I have a great deal to accomplish in a short period of time, I reach for paper and pen. When I have a great deal to do, I list the tasks to be accomplished, establish priorities, and try to set up a reasonable time frame in which to get them done. When my emotions have been tested, I make an entry in my diary. When I have spent a lot of myself and my energy on the needs and problems of others, I write a letter focusing on all that's good in my life. I view writing as a healthy form of transference. It purges my mind of information that interferes with action and helps to organize my thoughts into patterns of action.

Another essential change in my life has been learning to set reasonable goals and to reach them. (I still struggle with what's "reasonable.")

When I left the hospital, I felt as though I could do nothing. Reaching a goal wasn't even an issue when getting out of bed was my greatest challenge. I had no desire to set a goal because I had no desire to live.

To relieve her own pain of watching me waste away, my mother taught me to crochet. The goal was a poncho cape. She coached me while I struggled with a skein of wool which seemed to have no end. My therapist became a cheerleader along the sidelines, encouraging me to finish the cape, to do a row a week, and to bring it to his office for periodic checkups. It took 3 years, but I finished it! I won the game against that part of me that was already defeated.

In addition to mental purging and reasonable goal-setting, I have endeavored to remain mentally stimulated. At first I had the sense that I had suffered a mental (heart) attack—a stroke of the brain. My body movements were slow and mechanical; my brain functions were retarded. In general, I was on slow speed.

Not only was I painfully aware of the differences in my mental and physical abilities, but I felt helpless to rehabilitate myself. When I returned to work and to graduate school, I had great difficulty attending to lengthy oral instructions and concentrating on written material. In spite of the challenge, I endured. In time, especially after I discontinued medications, I was more academically proficient than I had been before my illness. Being back in school forced me to think about something other than myself. As a psychology graduate student, my course work put my illness into perspective, and my illness provided a special meaning and direction for my education and training.

When I returned to work, school, and the stresses of "normal" living, the importance of defining my own limits and setting reasonable goals became apparent. I learned through two subsequent episodes that I could not permit others to push me, and more importantly, that I could not push myself without suffering serious consequences. I learned that any change—such as a business trip or vacation—which drastically altered my routine was stressful. Deadlines, other- or self-imposed, were harmful, especially if they were unrealistic.

I had to learn that my body rhythm had been reset at a slower speed and that I could no longer work and play at my previous rate without suffering a physical or mental "breakdown." I was indeed much like the patient recovering from a heart attack. If I were to avoid another "attack," I had to change my physical pace and my mental attitude about myself and my abilities.

Socially, I also experienced changes and with these changes I had to learn new social skills which would not only help me but others to cope with my illness and hospitalization.

Because I was a mental health professional, I assumed that my colleagues would be intensely interested in my experiences as a patient. I felt no reason to closet myself because of my illness—I had done nothing wrong. I had gotten sick, had a mental (heart) attack. My desire to detach and withdraw grew more from a sense of physical ugliness than from my episode and hospitalization. I wanted and expected to be embraced for my suffering, not rejected because of it.

A condition, which I call "justifiable paranoia," developed from experiences of rejection (covert and overt), persecution, and discrimination. Others simply did not know how to relate to me as a recovering psychotic. Does one send a get-well or a thinking of you card? Does one visit? What does one say to a business associate who is shuffling around on Haldol? What tasks should a supervisor assign to an employee who is having feelings of uselessness? Can universities accredit students as psychologists who receive part of their education (without credit) in a mental hospital?

If not for *many* advocates (whom I will discuss later), I might not have been able to endure the answers to these questions. I was forced, for my survival, to learn—for the first time in my life—to fight. No longer could I turn the other cheek.

My friends have remained my friends. New acquaintances—people who accept me for my strengths, my weaknesses, tragedies, successes, and failures—are vitally important to me. They reassure me that "I'm OK." Those who continue to struggle for a sense of mental health, who call or write asking for hope, inspire me.

I have been told that some call me names, say I'm "crazy" and "unfit" to counsel young people. While these words hurt me deeply, I have acquired such a strong sense of self that they no longer interfere with my progress. I know who and what I am. I am sufficiently content to forgive them.

I am still learning how and when to say "no," "I can't," and "I don't want to." I have learned to speak about my illness only when I'm asked about it. I rarely volunteer my "confession" of sins as a mental patient. Most important, I've learned to laugh about my experiences, to say the word "crazy" and know that it doesn't apply to me. I have learned when to closet myself and when to open my closet door. Occasionally I even shake my skeleton and know that others are laughing with me and not at me.

In the emotional dimensions I have also had many lessons: I have learned to cry.

A few years after my illness I met someone who permitted me to talk about my hospitalization. As I described the experience, I cried. A gentle touch that said, "It doesn't matter; we can still be friends" was worth years of therapy. That moment was an emotional breakthrough for me. That person gave me a very precious gift—hope.

Many emotional lessons in anger have yet to be learned. I often "sit on it." It's there; I feel it; but I don't express it well. All too often it's displaced and misplaced. It's a problem I share with much of our society.

Former patients live in emotional straightjackets simply by the nature of their illness. To others, misplaced anger may be a sign of repressed violence. Tears, a state of sadness, may be misread as an impending state of depression. Laughter may be heard as mania. Emotional extremes create fear, especially in those who only know of our history rather than our personalities.

My spirit is stronger, more determined. It permits me to "tune in" to myself and the world around me.

Some of the most beneficial changes for maintaining my mental health have been environmental. Learning when to move has not been an easy lesson. It has always been costly financially but with a substantial benefit emotionally.

Six months after my hospitalization I decided to take a leave of absence from my job and live in Seattle, Washington, with friends. The time away was very therapeutic. I used it to write an overdue research paper for one of my graduate courses, to rest, relax, and assess my life. It helped me to see how the stresses of my everyday lifestyle had contributed to my illness.

The most crucial change for me occurred in the workplace about 2 years after my hospitalization. I moved from an office setting which was stifling and destructive to one which continues to be supportive and creative. In this new work environment I have found meaning to my life. I have been permitted to grow and develop with an abundance of nurturance, encouragement, and support.

Repeatedly, I have pointed out the importance of the workplace, particularly for the recovering patient. For most of us, the workplace is the primary source of ego strength. We spend our young life preparing to work and the majority of our awake, adult life at work. Some of us work by the Protestant ethic; others of us develop identities around job titles and organizational affiliations. We work to survive as well as to enjoy life. It is often a source of stress and a source of socializing. It provides our bread and butter, our meat and potatoes. Without a meaningful job, we lack meaning. We become parasites on society by chance rather than by choice. Worst of all, we have no self-worth.

I have been extremely fortunate in this regard. My education, training, and diversified work experiences occurred before my illness. I was hospitalized as a respected mental health professional and honor student in graduate school. There was a fair share of security attached to my job, and there were opportunities for career advancement before my illness.

My episodes and hospitalization undermined my own accomplishments. Not only was I experiencing a rebirth emotionally, physically, mentally, and socially, but I was as an infant in the arms of my employer.

My work and work environment had contributed significantly to my "breakdown," but I was ill equipped to move into a new job situation when I returned to work. At the same time that I needed to relocate organizationally, I was clinging to what was known and familiar to me.

In time, as I grew stronger and could recognize the destructive aspects of my work situation, I challenged the injustices. My struggle against management resulted in a most satisfactory job transfer to the Mental Health Study Center of the National Institute of Mental Health. The first steps toward the reconstruction of my dormant ego and infantile identity were taken when the Chief of the Child and Youth Programs Section, Dr. Milton Shore, reviewed my job application and resume, invited me in for an interview, expressed an interest in having me work *with* him, and engaged the system to hire me: It was as though he had injected me with hope.

The new job situation only improved over time. Special arrangements were made and approved for me to complete my graduate work while conducting research and providing counseling to students in a high school. My on-site supervisors, whom I subsequently told of my experiences as a mental patient, applauded my excellent work and assured me of a continued place on the staff. If there was discrimination, it was in my favor: My consulting assignments broadened to all areas of the school; my counseling caseload was increased; I was asked to develop staff training programs on sensitivity and caring. They rewarded me for my own intense sensitivity to kids and my ability to help them find solutions (rather than to "wallow" in problems). I set my own limits and priorities. I was given opportunities to translate my own personal tragedies into something meaningful for others.

Many people have served as my advocates these past 5 years. I have mentioned only a few of them here.

My family and friends have continued to give love in abundance. They coached, encouraged, cried, and laughed with me. They have been my army against those who were denying me my place as a productive, worthwhile member of society.

My therapist, Jeremy P. Waletzky, M.D., has become a friend. He has permitted me to be *his* teacher.

Norman Rosenberg, my attorney at the Mental Health Law Project, validated my sanity. He was my armor in the battles against a university which was denying me readmission to graduate school and against a supervisor who threatened me with disability retirement.

My supervisors have restored a sense of meaning and purpose to my life. By giving me a place to give to others, I believe they have given many places to many people like me.

The Author

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Poetry

Tomorrow
I'm going to
spew my emotions
into the largest
of Rubbermaid wastebaskets,
seal it
with Reynolds aluminum wrap,
and set
the hazardous urn
out for the trashman.
—Lynne Morris, 9/20/80

I open my mouth
and out flood
words of cowardice,
pouring over any listener
like an upset gallon
of bright yellow paint.

I wonder how easily
the listener removes
my words.

I feel like a nuisance,
overdramatizing the insecurities
other people manage
to understate.

I never learned
the paintbrush method
of dealing with fears.
—Lynne Morris, 9/20/80

I'm viewed
as an open can
of gasoline,
apt to explode
and burn someone
at any time,
and I'm aware of that
and hurt by that.

I'm viewed
as a helium balloon,
apt to pop or
drift away,
and I'm aware of that
and hurt by that.

I'm viewed
as honey,
apt to be sticky
if not
properly contained,
and I'm aware of that
and hurt by that.

The more you
view me
negatively,
the more I hurt,
and the more I hurt,
the more
I behave negatively,
and I'm aware of that
and hurt by that.

I'm viewed
as a cigarette,
a threat
to your health
and very expensive,
and I'm aware of that
and hurt by that.

I'm viewed
as a scarecrow,
apt to hurt
your reputation
if you talk to me,
and I'm aware of that
and hurt by that.

The more you
view me
negatively,
the more I hurt,
and the more I hurt,
the more
I behave negatively.
To my great
misfortune
I am a
person
who needs
people,
and I'm aware of that
and hurt by that.

—Lynne Morris, 9/9/80

I
am
the
rear tire
of a bicycle,
not trusted enough
to be a
front tire,
expected to go
round and round
in one narrow rut,
never going very far,
ignored
except
when I
break down.
Then
I get lots of
frightening,
angry
attention
and
I am put into
a
garage,
sometimes for months,
where
I forget my function
and
I become afraid
to function
and all functions seem useless.

Next time out
I think I will be
an off-ramp
from a
freeway.

—Lynne Morris, 9/8/80

Bibliography and Abstracts on Schizophrenia

The abstracts that appear below are drawn from the computer-based information storage and retrieval system operated by the National Clearinghouse for Mental Health Information. They were selected for inclusion here on the basis of their direct relevance to schizophrenia: judgments about the quality of the article or book abstracted have been left to the reader. Foreign titles have been translated and the city of the journal's origin noted. Languages that use neither the Latin nor Fraktur (German) alphabets (e.g., the Slavic languages) have been transliterated. Titles of articles, books, and infrequently cited journals have been translated from these languages, and all other identifying information appears in English in their citations.

This collection is not exhaustive. The Clearinghouse routinely scans all mental health related literature, and its information system includes references to a great many articles of potential use to readers who are involved with research, training, or treatment in schizophrenia. Many of these references—notably reports of basic research—may not be published in the *Bulletin,* but are available from the Clearinghouse in other publications or through individually generated bibliographies. Because *Psychopharmacology Abstracts* publishes a comprehensive list of new articles on drug trials in schizophrenia monthly, only those articles that review a number of psychopharmacological studies are published here. Mental health professionals or laypersons actively working in the mental health field who wish to request computer printouts of late references or comprehensive bibliographies on specific aspects of schizophrenia may write to the following address:

Technical Information Section, National Clearinghouse for Mental Health Information, National Institute of Mental Health, Rm. 11A21, 5600 Fishers Lane,
Rockville, MD 20857.

The articles described in these abstracts are not available from either the Clearinghouse or the Center for Studies of Schizophrenia.

Attention, Perception, and Cognition

4428. Freedman, J.E. (University of Arizona, Tucson, AZ 85721) A comparison of two backward masking methodologies with schizophrenics. Dissertation Abstracts International, 40(8): 3926–B, 1980.

Paranoid schizophrenics, nonparanoid schizophrenics, and normal control subjects were tested on two backward masking methodologies to assess their speed of perceptual processing. No significant differences among the three groups were found in their performance on either of the two tasks. When the subjects were separated into extreme paranoid and nonparanoid groups, the nonparanoid schizophrenic group processed information more slowly. These data failed to replicate earlier findings that schizophrenics tend to process information more slowly than normal controls. It remains unclear as to whether paranoid schizophrenics differ from comparable normal controls in information processing ability.—Journal abstract, modified.

4429. Haydon, M.H. (New York University, New York, NY 10003) Schizophrenic dysfunction in verbal processing. Dissertation Abstracts International, 40(11):5438–B, 1980.

Schizophrenic dysfunction in basic verbal processing stages was investigated, using techniques developed in experimental psychology to study normal information processing. A multiple-choice recognition test was used to probe paranoid and undifferentiated schizophrenics' ability to use contextual constraints selectively with respect to primary and secondary attributes of words. The effects of semantic and irrelevant distractors, imagery, concreteness, affectivity, and input and output cues on the efficiency of recognition memory in schizophrenic subjects were assessed. The performance of undifferentiated, reactive schizophrenic subjects (UR) was found to differ from both normal and other schizophrenic groups in that: 1) UR subjects were relatively insensitive to high versus low salience differences; 2) UR subjects showed an advantage for low over high concreteness and imagery for correct responses in the partially cued or noncued conditions; and 3) the UR subjects seemed uninfluenced by high affect. Performance of paranoid schizophrenics closely paralleled that of normal subjects. It is concluded that schizophrenics suffer from a functional encoding dysfunction, which manifests itself differently in each of the schizophrenic subtypes.—Journal abstract, modified.

4430. Mannuzza, S.; Spring, B.J.; Gottlieb, M.D.; and Kietzman, M.L. (Department of Psychophysiology, New York State Psychiatric Institute, 722 West 168th Street, New York, NY 10032) Visual detection threshold differences between psychiatric patients and normal controls. Bulletin of the Psychonomic Society, 15 (2): 69–72, 1980.

Visual detection thresholds of acute hospitalized psychiatric patients and nonpatients were obtained using an adaptive, criterion-free, three-interval, temporal, forced-choice, double-staircase procedure. In Experiment I, 23 schizophrenic patients and 13 nonpatient controls were tested; in Experiment II, 17 schizophrenic patients, 15 patients with major depressive disorder, 15 siblings of schizophrenic probands, and 18 nonpatient controls were tested. Results of both experiments indicated that patients required about twice as much luminous energy for absolute threshold detection, with about 50 percent overlap between patient and control distributions. Results suggest that there are differences in visual sensitivity between psychiatric patients and normal controls that cannot be attributed to response bias factors. (28 references)—Author abstract, modified.

4431. Mo, S. S., and Kersey, R. (Department of Psychology, University of Southern Colorado, Pueblo, CO 81001) Foreperiod effect on time estimation and simple reaction time in schizophrenia. Journal of Clinical Psychology, 36(1):94–99, 1980.

The effects of foreperiod duration (FP) on time estimation and reaction time were compared. There was no difference between schizophrenics and nonschizophrenics with respect to the effect of FP, or with respect to the effect of change in FP. Prior information about FP invalidated these two effects on schizophrenics' time estimation and had a detrimental effect on their reaction time. Alcoholics' time estimation and reaction time were affected little by such prior information. Suppression of preparation by expectancy is shown to be a possible characteristic of schizophrenia. (10 references)—Author abstract.

4432. Mo, S.S.; Kersey, R.; Childs, A.M.; and Huang, D.D. (Department of Psychology, University of Southern Colorado, Pueblo, CO 81001) Differential effect of prior event information on reaction time with respect to paranoid vs nonparanoid symptomatology. Journal of Psychiatric Research, 15(1):41–49, 1979.

The dichotomy between paranoid and nonparanoid schizophrenia was studied in terms of difference in direction of underlying informational processes. The effect on reaction time (RT) of prior information concerning the imperative stimulus was tested among 20 chronic undifferentiated schizophrenics and 20 paranoid schizophrenics. In three separate experiments, the RT of the chronic undifferentiated schizophrenics increased, and RT time of the paranoid schizophrenics decreased, when prior event information was provided. It is concluded that paranoid vs. nonparanoid symptomatology is based on two elementary processes which are dichotomous and characteristically different from each other. (11 references)—Author abstract, modified.

4433. Murchie, D. K., and Weckowicz, T.E. (Department of Psychiatry, Clinical Sciences Building, University of Alberta, Edmonton, Alberta, Canada T6G 2G3) Semantic priming in nonproductive schizophrenia. Journal of Communication Disorders, 13(4):249–261, 1980.

A group of 10 nonproductive schizophrenics—i.e., not experiencing hallucinations, delusions, or mood swings—was compared with a group of 10 nonpsychotic alcoholics, matched on visual acuity and reading level, in a primed-word identification task. Subsets of three target words were projected onto a series of screens constructed in such a way that an increasing random proportion of the words' features were made visible. The prime was the category to which the target words belonged; the target words represented one of four levels of goodness of membership in the primed category. On the whole, identification thresholds in the two groups were not significantly different. However, although the alcoholics' thresholds increased rapidly as goodness of membership decreased, this trend was not significant in the schizophrenic group. When the target words were poor members of the primed category, the schizophrenics' thresholds were significantly lower than the alcoholics'. Such results are consistent with Feigenberg's characterization of schizophrenia as a disturbance in the process of probabilistic prognosis. (23 references)—Author abstract.

Parkison, S.C. (Texas Tech University, Lubbock, TX 79409) The effects of distraction on the vigilance performance of paranoid and nonparanoid schizophrenics. Dissertation Abstracts International, 40(12): 5824–B, 1980.

The effects of distraction on the vigilance performance of paranoid and nonparanoid schizophrenic subjects were investigated, and two theories of attentional deficits in schizophrenia were evaluated. Sixty hospitalized schizophrenics—30 paranoid schizophrenics and 30 nonparanoid schizophrenics—participated in a 30-minute vigilance task, which was analyzed in six 5-minute blocks. Paranoid and nonparanoid schizophrenics did not differ on ability to perform during distraction; however, the groups did differ on attentional ability regardless of distraction. Implications for the theories of Silverman and Broadbent are discussed.—Journal abstract, modified.

4435. Pogue-Geile, M. F., and Oltmanns, T.F. (Department of Psychology, Indiana University, Bloomington, IN 47405) Sentence perception and distractibility in schizophrenic, manic, and depressed patients. Journal of Abnormal Psychology, 89(2):115–124, 1980.

The influence of distraction on cognitive performance was explored with eight schizophrenics, eight manics, eight depressives, and eight normal subjects. Subjects were asked to shadow short stories in both the presence and absence of a competing message and then answer questions about the content of the shadowed message. The shadowing performance of all three patient groups was equivalent to that of normal subjects and was not affected by distraction. Shadowing errors of commission showed that schizophrenics utilized semantic and syntactic information to anticipate words in the relevant message, but the schizophrenics also inserted more semantically irrelevant words than any of the other three groups. Distraction did interfere with the schizophrenics' ability to recall the content of relevant passages, but not with the performance of the other three groups. These data indicate that distraction may have a specific rather than general influence on controlled information processing or that distraction may reduce schizophrenics' overall capacity to handle information in short-term memory. The analysis of shadowing errors suggests that performance on such laboratory tasks may be closely related to the verbal communication problems encountered by many schizophrenic patients, but it also indicates that these symptoms may not be a simple function of selective attention difficulties. (30 references)

4436. Poole, A.D. (Department of Psychiatry and Behavioral Science, University of Western Australia, Nedlands, Western Australia 6009, Australia) The Grid Test of Schizophrenic Thought Disorder and psychiatric symptomatology. British Journal of Medical Psychology, 52(2): 183–186, 1979.

The relationship between the Grid Test of Schizophrenic Thought Disorder and various aspects of patient symptomatology and prognosis, other than clinical thought disorder, is studied. Seventy-five patients were given the Grid Test for diagnostic purposes. Data were also examined relating to the presenting symptomatology of each patient. Variables specifically selected for investigation were: delusions, hallucinations, depression, ideas of reference, obsessive compulsions, orientation, and memory. No significant associations, apart from a relationship between test performance and ideas of reference in schizophrenic patients, were obtained. It is concluded that the Grid Test has yet to be demonstrated to have any utility in the evaluation of symptomatology or prognosis. (9 references)

4437. Powell, D.A. (Washington State University, Pullman, WA 99163) The influence of linguistic redundancy in the language disturbance of schizophrenia. Dissertation Abstracts International, 40(7):3416–B, 1980.

A hypothesis was investigated as to whether a nonschizophrenic psychiatric group, such as depressives, and a schizophrenic subtype show the same inability to benefit from linguistic redundancy. Subjects were 48 inpatients equally divided into paranoid schizophrenics, nonparanoid schizophrenics, depressives, and nonpsychiatric medical patients. Each subject listened to and recalled four 25-word passages designed to independently highlight the semantic and syntactic components of linguistic redundancy. The results suggest that, when methodological improvements are made, no significant differences in performance on a redundancy task appeared, even between schizophrenics and nonpsychiatric patients. These findings indicate that the present redundancy task is not an effective means of diagnostic discrimination.—Journal abstract, modified.

4438. Rausch, M. A.; Prescott, T.E.; and DeWolfe, A.S. (Department of Psychology, Loyola University, 6525 North Sheridan Rd., Chicago, IL 60626) Schizophrenic and aphasic language: Discriminable or not? Journal of Consulting and Clinical Psychology, 48(1):63–70, 1980.

The linguistic performances of normal, process and reactive schizophrenic, and aphasic subjects were compared. To determine whether the subjects could be differentiated on their ability to apply linguistic rules, a word-ordering task was administered to 40 subjects. The results demonstrated that aphasic subjects could be differentiated from schizophrenics and normals by the task completion time and the number and type of errors. Process and reactive schizophrenics were not differentiated by the task. The performance of the schizophrenics was indistinguishable from that of the normal subjects on all but one measure. The schizophrenics differed from the normals in the number of errors in rearranging sentences involving both direct and indirect objects. (37 references)—Author abstract, modified.

4439. Russell, P.N.; Consedine, C.E.; and Knight, R.G. (Department of Psychology, University of Canterbury, Christchurch 1, New Zealand) Visual and memory search by process schizophrenics. Journal of Abnormal Psychology, 89(2):109–114, 1980.

The response times of 20 process schizophrenics—10 paranoid and 10 nonparanoid—and 20 nonhospitalized controls were compared on a hybrid visual and memory search task. Subjects searched displays of up to 15 letters, reporting whether or not displays contained a target, which was drawn from a memorized set of one, three, or six letters. Response times of all groups increased linearly with the product of the number in the memorized target set and the number of displayed letters. Although the intercepts and response times of the schizophrenics exceeded those of controls, no group differences were found in slopes or in rates of increase in response time as a function of the number of memorized or displayed items. Results are interpreted in terms of a model proposed by Schneider and Shiffrin, which states that process schizophrenics are retarded in processes associated with response production, but not in a variety of processing stages involved in the comparison of displayed and memorized information. (10 references.)—Author abstract.

4440. Saccuzzo, D.P., and Braff, D.L. (Department of Psychology, San Diego State University, San Diego, CA 92182) Associative cognitive dysfunction in schizophrenia and old age. Journal of Nervous and Mental Disease, 168(1): 41–45, 1980.

Chapman's matched associative distractor test was used to determine whether an associative dysfunction is unique to the schizophrenias. Schizophrenic and control subjects were administered two matched multiple choice subtests, with only one containing an incorrect alternative choice. Only the schizophrenics and the institutionalized elderly made significantly more errors on the associative subtest than on the nonassociative subtest. The results indicate the vulnerability to associative distractors is not a unique pathological response pattern of schizophrenia, and adds support to the knowledge that many of the pathognomonic dysfunctions associated with schizophrenia are also found in other groups. (26 references)—Author abstract.

4441. Schelling, U. (Rehabilitationszentrum Rudolf-Sophien-Stift, Leonbergerstr. 220, D-7000 Stuttgart, Germany) Structure, levels and deficiencies regarding the abilities of schizophrenics. Fortschritte der Neurologie-Psychiatrie und ihrer Grenzgebiete, 48(5):249–266, 1980.

The performance of 105 schizophrenic patients was tested in 22 cognitive, psychomotor, and general ability tests and compared with that of a normal control group. In most tests, the schizophrenic patients were inferior in verbal and nonverbal intelligence, manual dexterity and speed, reaction time, concentration, coordination, and susceptibility to interference. Test performances correlated positively with previous school and job training and with the father's professional position. There was a negative correlation with the duration of present and past hospitalizations and the ratings of ward behavior, and with neuroleptic sedation. Enhanced interindividual variability of performance was largely clarified via subclassification of the patients by cluster analysis using their test profiles as a basis. The results are discussed in terms of motivation and rehabilitative consequences and the effects of the interactions between the patient and the hospital. (32 references)—Journal abstract, modified.

4442. Schneider, P.A. (Rutgers University, 92 New Street, Newark, NJ 07102) Schizophrenic listener performance in a referent communication task. Dissertation Abstracts International, 40(7):3492–B, 1980.

Two models of the process in which listeners might choose which stimulus object is a speaker's referent were examined using schizophrenics and normals as subjects. The suspended judgment model—e.g., in which subjects choose rationally among all alternatives—was consistent with normals' choice latencies when the perceptual problems were minimal. However, under perceptually demanding conditions, the normal's choice latencies were a linear function of the associative strength of the color pair as possible referents of the descriptor. In the impulsive judgment model—e.g., in which subjects select the first alternative which seems applicable—schizophrenics' shortest latencies were in the minimal perceptual problems condition and their longest in the high. Schizophrenics also made faster choices than normals in all conditions. It is suggested that this relative speed is an expression of a tendency to escape from aversive situations.—Journal abstract, modified.

4443. Schubert, D.L. (California School of Professional Psychology, San Diego, CA 92138) Information processing deficit in affective disorder. Dissertation Abstracts International, 40:(8):3967–B, 1980.

In an investigation of an affective disorder deficit in the early stages of information processing, backward masking functions were compared for three psychotic groups—eight schizoaffective, eight manics, and eight major depressives—and two matched control groups—eight minor depressives and eight hospital personnel. In a forced-choice letter recognition procedure, critical stimulus duration was assessed, and criterion accuracy was determined for 4-msec and 6-msec test stimulus durations when followed by blank and pattern-masking stimuli. Results indicated that the three psychotic groups required significantly longer stimulus duration, as well as significantly longer masking intervals for criterion accuracy than the control groups. Results are interpreted as indicating that the central processing deficit documented in schizophrenia also occurs in the affective disorders.—Journal abstract, modified.

4444. Shanker, P. (Department of Psychology, 515 Portage Avenue, Winnipeg, R3B 2E9, Canada) Perception of the upright in normal and schizophrenic subjects. Perceptual and Motor Skills, 50(1):104–106, 1980.

The perception of the upright was examined in 24 normal and 24 schizophrenic subjects. A large angle of frame tilt with movement of a rod in the clockwise direction in a darkened room was used. The results showed a small error with a clockwise movement of the rod, when the frame also was tilted clockwise, and no difference in perception of the upright between the normal and schizophrenic subjects. (5 references)—Author abstract, modified.

4445. Staugaitis, S.D. (No address given) Attentional deficit in acute schizophrenics and normals as a function of stimulus-interference, response-interference and field articulation. Dissertation Abstracts International, 41(1):370–B, 1980.

Attentional deficits in acute schizophrenic and normal subjects were investigated as a function of stimulus interference, response interference, and field articulation. An experimental task was developed which systematically manipulated stimulus interference by varying the number of distractors present in the visual field from which one relevant stimulus had to be located. Response level interference was manipulated by presenting two classes of relevant stimuli—nonsense syllables and color words. Results demonstrate significant delay for the schizophrenic group in comparison to the control subjects in the presence of both stimulus interference and response interference. In addition, field articulation was found to be significantly related to stimulus interference, but unrelated to response level interference.—Journal abstract, modified.

4446. Steffy, R.A., and Galbraith, K.J. (Department of Psychology, University of Waterloo, Waterloo, Ontario, Canada N2L 3G1) Relation between latency and redundancy-associated deficit in schizophrenic reaction time performance. Journal of Abnormal Psychology, 89(3):419–427, 1980.

The independence of two measures of information processing difficulties in process schizophrenics--the reaction time (RT) measures of latency and redundancy-associated deficit—was investigated. Training exercises were used to improve the speed of RT of schizophrenics, and they were successful in reducing latency over the course of training and from pretraining to posttraining assessment. Redundancy-associated deficit did not change from preassessment to postassessment. Intercorrelations of the two indexes showed that these measures were independent, at least within the process end of the schizophrenic spectrum. Both measures correlated with different types of subject factors. Latency measures correlated with those of chronicity, while the redundancy-deficit measure correlated with prognosis. These findings help to clarify the utility of various RT indexes as markers of various aspects of schizophrenic pathology. (33 references)—Author abstract, modified.

4447. Thimmappa, M.S. (Department of Psychology, Bangalore University, Bangalore 560056, India) Conditioning and verbal learning in psychiatric patients (an experimental study with schizophrenics). Indian Journal of Clinical Psychology, 6(1):7–11, 1979.

To investigate the nature of sensory, verbal, and symbolic learning in schizophrenia, conditioning and verbal learning were measured in a group of 30 chronic schizophrenics, 15 anxiety neurotics, and 50 normal subjects. All three groups were similar in their age and educational level. Classical aversive conditioning and verbal learning consisting of three lists of paired-associate nonsense syllables and words of various degrees of difficulty and verbal concept learning tasks were used to investigate sensory and symbolic learning. In all of the tasks there was a significant difference between schizophrenics and normals, and schizophrenics and neurotics, but no significant difference between normals and neurotics. Schizophrenics took more trials to learn than normals and neurotics. (19 references)—Author abstract, modified.

4448. Wahl, O.F., and Sieg, D. (George Mason University, 4400 University Drive, Fairfax, VA 22030) Time estimation among schizophrenics. Perceptual and Motor Skills, 50(2):535–541, 1980.

Time estimation among schizophrenics was examined using several methods of time estimation within the same study and maintaining a consistent definition of overestimation and underestimation across tasks. Twenty-six schizophrenic and 26 control subjects were given three types of time estimation tasks—longer interval estimation, verbal estimation, and operative estimation. Schizophrenic subjects were significantly more inaccurate than controls in the verbal and operative estimation tasks. In addition, they were significantly more likely to overestimate. These results indicate that schizophrenics experience real time as passing more slowly than is actually the case. (12 references)—Author abstract, modified.

Biology

4449. Arora, R.C., and Meltzer, H.Y. (Illinois State Psychiatric Institute, 1601 West Taylor St., Chicago, IL 60612) Muscle cholinesterase: Effect of phencyclidine and ketamine on rat and human muscle cholinesterase activity. Experimental Neurology, 67(1):1–10, 1980.

The effects of phencyclidine (PCP) and ketamine on rat skeletal muscle acetylcholinesterase (AChE) activity and the effects of PCP on AChE activity of skeletal muscle from schizophrenic and normal subjects were studied. Both drugs weakly inhibited rat skeletal muscle AChE activity and human muscle AChE activity in vitro. In vivo, both drugs stimulated rat skeletal muscle AChE activity, but no effect was observed on rat brain AChE activity. When combined with restraints for 30 minutes following PCP and ketamine, the stimulation of AChE activity was greater than that produced by drug alone or restraint alone. No difference in the ability of PCP to inhibit AChE activity of skeletal muscle from schizophrenic patients compared to normal controls was noted. (25 references)—Author abstract, modified.

4450. Bernstein, A.S.; Schneider, S.J.; Juni, S.; Pope, A.T.; and Starkey, P.W. (Department of Psychiatry, State University of New York, Downstate Medical Center, 450 Clarkson Avenue, Brooklyn, NY 11203) The effect of stimulus significance on the electrodermal response in chronic schizophrenia. Journal of Abnormal Psychology, 89(1):93–97, 1980.

Skin conductance reactivity (SCR) to stimuli was compared in schizophrenics, normals, and alcoholics. Trials began with a 5-second slide presenting four different words and ended 15 seconds later with a recorded auditory presentation of one of these words. For half of each sample, stimuli were made significant by requiring subjects to retain the visually given words so that, on hearing the subsequent spoken word, they could immediately repeat one of the words in the last seen slide other than that just heard (report condition). The remaining subjects only had to sit still and do nothing (simple condition). As predicted, schizophrenics showed smaller, faster habituating SCRs than controls only in the simple condition, and resembled controls when the same stimuli were made significant in the report condition. In all groups, introducing explicit significance markedly increased SCR amplitude, slowed habituation, and heightened spontaneous fluctuation frequency to both visual and auditory stimuli, but did so most markedly to the auditory signals that were closer in time to the significance creating report. (18 references)—Author abstract, modified.

4451. Cooper, S.; Albert, J.–M.; Dugal, R.; Bertrand, M.; and Elie, R. (Institut National de Recherche Scientifique-Sante, 7401, rue Hochelaga, Montreal H1N 3M5, Quebec, Canada) Gas chromatographic determination of amitriptyline, nortriptyline, and perphenazine in plasma of schizophrenic patients after administration of the combination of amitriptyline with perphenazine. Arzneimittel-Forschung, 29(1):158–161, 1979.

A specific and sensitive gas chromatographic technique, using a common extraction procedure, for the determination of amitriptyline, endogenous nortriptyline, and perphenazine in plasma of schizophrenics receiving both drugs is described. Lower limits of detection are 20 ng/ml, 1 ng/ml, and 5 ng/ml for amitriptyline, nortriptyline, and perphenazine, respectively. Amitriptyline was estimated with a flame ionization detector. Nortriptyline and perphenazine were quantitated using an electron capture detector. In individual patients, steady state plasma levels ranged from 44 to 215 ng/ml for amitriptyline, 49 to 270 ng/ml for nortriptyline, and less than 5 to 20 ng/ml for perphenazine. Steady-state plasma level data for 23 patients on a combined drug regimen are presented. (21 references)—Author abstract, modified.

4452. Cox, S.M., and Ludwig, A.M. (Department of Psychiatry, University of Kentucky College of Medicine, Lexington, KY 40506) Neurological soft signs and psychopathology: I. Findings in schizophrenia. Journal of Nervous

and Mental Disease, 167(3):161–165, 1979.

Systematic, standardized evaluations for neurological soft signs were conducted on five psychiatric populations and a control group of medical inpatients. Soft signs were grouped according to their probable clinical association with cortical lobe dysfunction. Preliminary results indicate that schizophrenics, compared to other groups, show significant increased presence of soft signs presumably related to frontal and parietal lobe dysfunction. (14 references.)—Author abstract.

4453. Dimond, S.J.; Scammell, R.; Pryce, J.; Huws, D.; and Gray, C. (Department of Psychology, University College, P.O. Box 78, Cardiff CF1 1XL, Wales) Some failures of intermanual and cross-lateral transfer in chronic schizophrenia. Journal of Abnormal Psychology, 89(3):505–509, 1980.

The suggestion that split brain symptoms are present in schizophrenia was investigated by using tests of intermanual and cross-lateral transfer. Disconnections were seen on a variety of intermanual and cross-lateral transfer tasks involving position location on the hands, arms, and body, as well as on tasks of manual tapping transfer. Findings are interpreted as communication failures of the brain related to callosal disturbance. (7 references)—Author abstract.

4454. Dohan, F.C. (Department of Molecular Biology, Eastern Pennsylvania Psychiatric Institute, Philadelphia, PA 19129) Schizophrenia and neuroactive peptides from food. Lancet, I(8124):1031, 1979.

In a reply to a critique by Horrobin (1979), the association between neuroactive peptides from food and schizophrenia is reviewed. It is noted that cereal grains and probably some other foods play a genetically determined causal role in schizophrenia, a fact based on empirical data and clinical observation including epidemiological/food consumption data and a possible genetic relationship between schizophrenia and celiac disease. Further, wheat gluten has been found to reverse the beneficial effects of a diet totally free of cereal grains and milk. While endorphin-like substances may be involved in the pathogenesis of schizophrenia, it is suggested that the neuroactivity of other, nonendorphin, food derived peptides also be investigated. While disturbed prostaglandin activity may occur, it is possible that the basic biological defect may be a genetic impairment of the gut and other barrier systems which eases the passage of neuroactive polypeptides from gut lumen to brain. (10 references)

4455. Domschke, W.; Dickschas, A.; and Mitznegg, P. (Department of Medicine, University of Erlangen-Nurnberg, Erlangen, Germany) C.S.F. beta-endorphin in schizophrenia. Lancet, I(8124):1024, 1979.

A study of cerebrospinal fluid (CSF) β-endorphin in five acute paranoid schizophrenic inpatients is reported. An additional seven chronic schizophrenics in a predominantly defective residual state and receiving neuroleptics and 10 controls with neurological symptoms were also evaluated. Results indicate that acute schizophrenics presented with immunoreactive CSF β-endorphin concentrations about 10 times higher than those of controls. In contrast, β-endorphin levels in chronic schizophrenics are about 50 percent of normal. Data are compatible with the view that altered endorphin homestasis does play a role in acute as well as in chronic schizophrenic states. It is concluded that analysis of CSF β-endorphin may prove helpful clinically in differential diagnosis. (9 references)

4456. Eckert, B; Gottfries, C.G.; von Knorring, L.; Oreland, L.; Wiberg, Å.; and Winblad, B. (Department of Pharmacology, University of Umea, S-901 87 Umea, Sweden) Brain and platelet monoamine oxidase in mental disorders. I. Schizophrenics and cycloid psychotics. Progress in Neuro-Psychopharmacology, 4(1): 57–68, 1980.

Monoamine oxidase (MAO) activity was examined in brains of 25 psychotic patients, 12 of whom fulfilled the criteria of Bleuler for schizophrenia and four of whom were classified as cycloid psychotics. No differences between controls and schizophrenics were found. The cycloid psychotics, however, had lower activities of MAO in most parts of the brain. MAO activity was also examined in platelets in schizophrenics (n = 14), hospitalized controls (n = 14), and healthy volunteers (n = 14). No significant differences were found between these groups; neither were any differences found in platelet MAO activity between alcoholic schizophrenics (n = 11) and healthy volunteers (n = 11). When platelet MAO activity in cycloid psychotics (n = 20) was compared to that in patients with unipolar affective disease, the cycloid psychotics were found to have significantly lower activities. It is suggested that differences in the classification of this disease may explain the inconsistent findings in regard to platelet MAO activity in schizophrenics. (44 references)—Author abstract, modified.

4457. Horrobin, D.F. (Clinical Research Institute of Montreal, Montreal, Quebec H2W 1R7, Canada) Prostaglandins and schizophrenia. Lancet, I(8124):1031–1032, 1979.

The association between schizophrenia and specific defect in 1-series prostaglandins with normal/near normal 2-series production leading to an imbalance between the two groups of compounds is examined. Research with paracetamol, which inhibits formation of both series-1 and series-2 prostaglandins, does not invalidate this proposed association. A brief critique of comments by Checkley and Slade (1979) on a study by Kay and Roth (1961) is also provided, and it is suggested that blindness in genuine schizophrenia is uncommon, and that blind individuals with schizophrenic features may sometimes have a common cause for both mental and visual impairment such as zinc deficiency. (7 references)

4458. Horvath, T., and Meares, R. (Department of Psychiatry, Stanford University, Stanford, CA 94305) The sensory filter in schizophrenia: A study of habituation, arousal, and the dopamine hypothesis. British Journal of Psychiatry, 134:39–45, 1979.

Habituation of the orienting response was used to investigate the possible failure of a notional sensory filter in schizophrenia. Nonparanoid schizophrenics failed to habituate, but paranoids habituated normally. Paranoids, however, showed a different impairment: They responded to a dishabituating tone as if the novel stimulus was somewhat familiar. The failure of habituation in nonparanoids could not be explained as arousal when the index was the rate of skin conductance fluctuation. Neurotic controls showed considerably higher levels than either group of schizophrenics. It is suggested that nonparanoid schizophrenics had lost the normal inverse relationship between habituation and level of arousal as manifested in the rate of spontaneous skin conductance fluctuation. (21 references)—Author abstract.

4459. Kari, I.; Rapakko, S.; and Airaksinen, M.M. (Department of Pharmacy, University of Kuopio, PO Box 138, SF-70101 Kuopio 10, Finland) Effect of some β-carbolines on phenylethylamine and apomorphine stereotypies in rats. Pharmacology Biochemistry and Behavior, 12(6):979–982, 1980.

The effects of tetrahydro-β-carbolines (THBCs) and some other β-carbolines were studied on the stereotypies caused by apomorphine (APO) and phenylethylamine (PEA) in rats. These effects of dopaminergic drugs like apomorphine as well as of PEA have sometimes been used as animal models of paranoid schizophrenia. Dose effect relationships were studied from the most potent substances. All β-carbolines studied significantly inhibited APO stereotypy. The most effective was 6-methoxyharmalan, followed by β-carboline (BC), tetrahydro-β-carboline (THBC), 1-methyl-THBC, y-methoxy-THBC, and 6-hydroxy-THBC. Also, 6-methoxyharmalan, 6-hydroxy-THBC, and BC also inhibited PEA stereotypy. Results indicate that the mode of PEA and APO stereotypies seems to differ, and β-carbolines seem to influence these stereotypies by more than one mechanism. If the dopamine hypothesis is valid, the β-carbolines formed in humans may protect rather than be detrimental in paranoid psychoses. (36 references)—Author abstract, modified.

4460. Miller, R.J. (Department of Pharmacological and Physiological Sciences at the University of Chicago, Chicago, IL 60637) From analgesia to schizophrenia: The potential of endorphins. Behavioral Medicine, 6(5):30–33, 1979.

The discovery in the nervous system of morphine-like peptides and their receptors and the pharmacological activities of these substances are discussed. Two major discoveries are discussed: the confirmation of the existence of opiate receptors and the discovery of the endorphins and the enkephalins, the peptides with a morphine-like action. Research on the role of opiate peptides in many areas of neurobiology and neuropharmacology is discussed. The discovery of the enkephalins also raises the possibility of producing an analgesic drug that is nonaddictive. Among the other functions of enkephalins are effects on gut motility. Studies being conducted to help clarify the roles of these peptides in normal and pathological states (e.g., schizophrenia and epilepsy) are cited. (3 references)

4461. Nachshon, I. (Department of Criminology, Bar-Ilan University, Ramat-Gan, Israel) Hemispheric dysfunctioning in schizophrenia. Journal of Nervous and Mental Disease, 168(4):241–242. 1980.

Data on hemispheric dysfunctioning in schizophrenia reported in a 1977 article are reinterpreted. The original data were analyzed using an attentional model, but new evidence regarding the relationship between psychopathology and laterality suggests the need for a new basis. This evidence shows greater right ear superiority effects for schizophrenics than for normal controls in dichotic listening and supports the assumption of left hemispheric overactivation among schizophrenics. This overactivation seems more pronounced among paranoid than among nonparanoid subjects. (33 references)—Author abstract, modified.

4462. Perez-Cruet, J.; Waite, J.G.; and Mehta, S. (Missouri Institute of Psychiatry, University of Missouri-Columbia School of Medicine, St. Louis, MO 63166) Pharmacokinetics of fluphenazine decanoate. (Abstract) Clinical Pharmacology and Therapeutics, 25(2):241, 1979.

A new fluorimetric method was used to measure fluphenazine plasma levels in eight schizophrenic patients 1, 2, 3, 5, 7, 9, 11, and 14 days after depot intramuscular injection of fluphenazine decanoate. Results indicated slow and variable release of fluphenazine from the depot site. Patients showed plasma drug peaks as early as 3 days or as late as 11 days after injection. No relationships between plasma levels of homovanillic acid and fluphenazine were observed.—Author abstract, modified.

4463. Rimon R.; Halonen, P.; Puhakka, P.; Laitinen, L.; Marttila, R.; and Salmela, L. (Department of Psychiatry, University of Helsinki, SF–00180, Helsinki, Finland) Immunoglobulin G antibodies to herpes simplex type 1 virus detected by radioimmunoassay in serum and cerebrospinal fluid of patients with schizophrenia. Journal of Clinical Psychiatry, 40(5):241–243, 1979.

Serum and cerebrospinal fluid specimens from 16 schizophrenic patients and 18 nonpsychiatric controls were tested by radioimmunoassay for immunoglobulin G antibody of capsid, envelope, and excreted antigens of herpes simplex type 1 virus. There were no significant differences in the antibody levels between the schizophrenic patients and the controls. The etiological role of viruses and virus-like agents in schizophrenia is discussed. It is suggested that the present evidence provides no support for the proposed role of viral agents in the etiology of schizophrenia. Methodological aspects of the problem are examined. (21 references)—Author abstract, modified.

4464. Rinieris, P.; Christodoulou, G.N.; Souvatzoglou, A.; Koutras, D.A.; and Stefanis, C. (Department of Psychiatry, Athens University Medical School, Eginition Hospital, 74 Vas. Sophias Avenue, Athens 611, Greece) Free-thyroxine index in schizophrenic patients before and after neuroleptic treatment. Neuropsychobiology, 6(1):29–33, 1980.

The mean values of serum thyroxine (T_4) *in vitro* radioactive triiodothyronine uptake and free thyroxine index (FTI) in 41 drug-free schizophrenic patients were determined. The values did not differ significantly from those of euthyroid controls. Following 6 weeks of treatment of 24 schizophrenics with chlorpromazine, trifluoperazine, or clozapine, a significant decrease in serum T_4 and FTI was noted after chlorpromazine and clozapine, whereas after trifluoperazine only serum T_4 decreased, but not FTI. The questions arising from these findings are discussed, and the need for a future investigation of serum triiodothyronine and serum thyroid stimulating hormone in schizophrenic patients before and after neuroleptic treatment is stressed. (21 references)—Author abstract, modified.

4465. Rist, F., and Cohen, R. (No address given) Paradoxical re-

sponse reduction and the flattening of affect in schizophrenia (Abstract). Psychophysiology, 16(2):201, 1979.

To examine paradoxical response reduction and flattening of affect in schizophrenia, heart rate (HR) and skin conductance (SC) were measured in chronic schizophrenic patients, alcoholic patients, and normal controls during a task that used verbal material of different affective connotation. Subjects were presented with pairs of words for 7 seconds (presentation phase). In the following 7-second interval (processing phase), subjects either had to choose one of these words on the basis of a clue word that had been provided, or to produce a clue word that matched a designated word of the pair. Results showed that schizophrenics responded to the affective significance of the stimuli, and responded equally to the two levels of task demand. Both comparison groups were more responsive when they had to produce the clue word. Results suggest that schizophrenics respond to affective challenge even when they are unresponsive to cognitive challenge. Ratings on the Brief Psychiatric Rating Scale of Overall and Gorham were obtained for schizophrenic patients. Principal components analysis yielded two factors which corresponded to cognitive disturbance and flattening of affect. It was shown that inhibitory processes were involved in flattening of affect.—Author abstract, modified.

4466. Roberts, M.A. (148–01 33rd Avenue, Flushing, NY 11354) Some possible pathways for the synthesis of trans-3-methyl-2-hexenoic acid. Journal of Orthomolecular Psychiatry. 9(2):129–134, 1980.

The literature concerning the odor associated with schizophrenia is reviewed, including identification of the malodorous compound as trans-3-methyl-2-hexenoic acid. It is suggested that faulty identification measures were used by those who suggest the compound as a causative agent and that a host of compounds may serve as logical precursors to the acid. Phenylalanine, 2-hydroxydopamine, and some unusual catechols are among these possibilities. One possible precursor, dopamine, has been described in the biochemical and psychopharmacological literature. It is concluded that new avenues of research should be opened into the possible biochemical etiology of the schizophrenic syndrome. (29 references)—Author abstract, modified.

4467. Roemer, R.A.; Shagass, C; Straumanis, J.J.; and Amadeo, M. (Eastern Pennsylvania Psychiatric Institute, Henry Avenue at Abbottsford Road, Philadelphia, PA 19129) Somatosensory and auditory evoked potential studies of functional differences between the cerebral hemispheres in psychosis. Biological Psychiatry, 14(2):357–373, 1979.

Results obtained by analyzing measures of the stability of auditory evoked potentials (AEPs) and somatosensory evoked potentials (SEPs) to determine the extent to which the visual evoked potential (VEP) evidence of left hemisphere involvement in schizophrenia may generalize to other sensory modalities are reported. Main findings were: (1) Overtly psychotic schizophrenics exhibit lower than normal stability in left hemisphere AEPs; (2) both overtly psychotic and latent schizophrenics show lower than normal waveform stability, bilaterally, in the later epoch of AEPs; (3) a subgroup of overt schizophrenics other than chronic paranoid or chronic undifferentiated had lower than normal stability in SEPs evoked by right median nerve stimuli and recorded from the right ipsilateral hemisphere. It is concluded that only the AEP results augment the previous VEP evidence indicating left hemisphere involvement in schizophrenic dysfunction. (18 references)—Author abstract, modified.

4468. Thimmappa, M.S. (Department of Psychology, Bangalore University, Bangalore 560056, India) Level of arousal in psychiatric patients (an experimental study with schizophrenics). Indian Journal of Clinical Psychology, 6(1):1–6, 1979.

Levels of autonomic arousal and cortical arousal were measured in a group of 30 chronic schizophrenics, 15 anxiety neurotics, and 50 normal subjects by means of the GSR skin resistance and spiral aftereffect tests. Lowered autonomic responsiveness to stimulation and increased cortical arousal were found in both schizophrenics and neurotics. It is suggested that the heightened arousal of chronic schizophrenics is due to the lack of discharge of internal excitations and subsequent withdrawal. (9 references)—Author abstract, modified.

4469. Tourney, G., and Erb, J.L. (University of Mississippi School of Medicine, Dept. of Psychiatry and Human Behavior, Jackson, MS 39216) Temporal variations in androgens and stress hormones in control and schizophrenic subjects. Biological Psychiatry, 14(2):395–404. 1979.

Radioimmunoassay techniques were used to study the steroid hormones dehydroepiandrosterone (DHEA), cortisol, testosterone, and androstenedione in schizophrenic and control subjects. Observations were made at four different times during the day. Cortisol, testosterone, and androstenedione demonstrated no significant differences between the two subject groups. DHEA was significantly below normal in the morning for the schizophrenic group, but within the range of the controls for subsequent determinations during the day. Control subjects showed a similar circadian secretion pattern for both DHEA and cortisol. It is reported that schizophrenics show almost the same circadian secretion patterns for cortisol as do the controls. (22 references)—Author abstract.

4470. Tyrrell, D.A.J.; Parry, R.P.; Crow, T.J.; Johnstone, E.; and Ferrier, I.N. (Clinical Research Centre, Northwick Park Hospital, Harrow, Middlesex HA1 3UJ, England) Possible virus in schizophrenia and some neurological disorders. Lancet, No. 8121: 839–841, 1979.

To determine whether there are common viruses in the cerebrospinal fluid (CSF) of acute schizophrenic patients, both schizophrenics and patients with a variety of other conditions were studied. Throat swabs, feces, paired sera, and CSF samples were collected from schizophrenic patients. From the other patients, only CSF was obtained. Results show that CSF from 13 of 18 schizophrenic patients has a cytopathic effect in cultures of MRC5 cells. The cytopathic agent passes a 100 nm, but not a 50 nm filter, and is unaffected by heat at 56°C for 30 minutes, treatment with chloroform, or the presence of cultures in bromodeoxyuridine. The agent cannot be propagated serially, but its properties are those of a virus. A similar cytopathic effect was induced by CSF from 8 of 11 patients with serious or chronic nervous system disease, but only 1 of 25 patients with surgical or general conditions. (12 references)—Author abstract, modified.

4471. Weinberger, D.R.; Torrey, E.F.; and Wyatt, R.J. (St. Elizabeths Hospital, Washington, DC 20032) Cerebellar atrophy in chronic schizophrenia. Lancet, No. 8118:718–719, 1979.

A study finding that chronic schizophrenic patients evaluated by computerized tomography (CT) had abnormalities of cerebral morphology is reported. Among the 60 chronic schizophrenic patients studied, a subgroup of 10 with possible lesions of the cerebellum was revealed. Research indicates that the cerebellar vermis is linked anatomically and functionally to areas of the limbic system that have been implicated in schizophrenia. It is concluded that researchers looking at CT scans of schizophrenic patients should check for cerebellar, especially vermian, atrophy and that postmortem studies are also needed. (10 references)

Cross-Cultural Studies

4472. Pull, C.B.; Pichot, P.; and Overall, J.E. (Clinique des Maladies Mentales et de l'Encephale, Paris, France) Comparison of French and American diagnostic practices for schizophrenia and depressive disorders. Psychopharmacology Bulletin, 16(2):43–46, 1980.

The diagnostic concepts and practices used by French and American psychiatrists in the diagnosis of schizophrenia and depressive disorders were investigated. Results confirm the fact that American diagnostic practices give a much broader definition to schizophrenia than do French and British practices. In contrast to a previous United States/United Kingdom study, the data of the American/French study clearly do not suggest that the American psychiatrists are diagnosing schizophrenia more frequently than affective disorder. The French diagnostic concepts of chronic hallucinatory psychosis and bouffée delirante are identified as the primary bases for more frequent use of the diagnosis of schizophrenia by American psychiatrists, even though they do not account for all of the differences. (12 references)

Description

4473. Akhtar, S.; and Thomson, J.A., Jr. (Department of Psychiatry, Jefferson Medical College, 1025 Walnut Street, Philadelphia, PA 19107) Schizophrenia and sexuality: A review and a report of twelve unusual cases—Part II.

Journal of Clinical Psychiatry, 41(5):166–174, 1980.

A review of schizophrenia and sexuality is presented and documented with 12 unusual cases. It is suggested that disordered sexual behavior is common in schizophrenia. Although some of this may be secondary to disturbances of thought and perception, the relationship seems far from absolute. The disturbances of subjective experience as well as those in overt sexual behavior may both come from a single cause—the breakdown of higher inhibitory functions that permit primitive sexuality to emerge, rather than one being the cause of the other. A greater knowledge of the sexual symptoms of schizophrenia may be utilized to sharpen diagnostic sensitivity to the incipient forms of the disorder; to estimate prognosis in a given case; to consider alternatives in treatment; and, perhaps, to understand more sexual crimes. (139 references)

4474. Angermeyer, M.C., and Timpe, F.H. (Medizinische Hochschule Hannover, Karl-Wiechert-Allee 9, D-3000 Hannover 61, Germany) Psychopathology and language behavior in schizophrenics. Archiv für Psychiatrie und Nervenkrankheiten, 228(2):151–160, 1980.

Verbal samples of 30 schizophrenics were analyzed using the Social Alienation-Personal Disorganization (Schizophrenic) Scale developed by Gottschalk and Gleser. The psychopathological status of all patients had been assessed in a semistandardized interview. A relatively close relationship was found between productive or plus symptoms and syndromes of psychosis and the scores on the content analytic scale. However, no significant relationship existed with the minus symptomatology and no relationship with the residual syndrome and the neurotic syndromes. It is suggested that the Schizophrenic Scale may allow a sufficiently reliable estimate of the degree of psychosis. There was no significant effect attributable to sociodemographic factors and to the course of illness, disregarding the duration of the present hospitalization. (25 references)—Author abstract.

4475. Beck, M.A., and Callahan, D.K. (United Cerebral Palsy Center, Suffolk County Committee, New York, NY 10001) Impact of institutionalization on the posture of chronic schizophrenic patients. American Journal of Occupational Therapy, 34(5):332–335, 1980.

The impact of institutionalization on the posture of chronic, undifferentiated schizophrenic patients was examined by dividing a sample of patients into a group of subjects who had been continuously institutionalized and a group who had been intermittently institutionalized. Patients who had been hospitalized for a longer, continuous period had significantly poorer posture than those who were institutionalized for a similar but intermittent period of time. It is suggested that poor posture seems to be a nosocomial condition arising from institutionalization, rather than arising from the illness the patient brings into the hospital. However, therapists need to examine possible types of therapeutic intervention with schizophrenic clients before selecting a sensory integration approach or one based on environmental considerations. (26 references)—Author abstract, modified.

4476. Bucher, R.E., and Terzis, A. (Departamento de Psicologia, Universidade de Brasilia, 70910 Brasilia, D.F. Brazil) Birth order and sibling relationships of schizophrenics. Arquivos de Neuro-Psiquiatria, 38(1):53–64, 1980.

Birth order and sibling relationship data from 150 schizophrenic patients were compared with data from a nonschizophrenic, psychiatric patient control group. No significant difference was found in birth order. Among males, 35.7 percent of alcoholics and 24.5 percent of schizophrenics were firstborns; among females, 17.2 percent of neurotics and 8.6 percent of schizophrenics were first-borns. A significant effect for sex of the preceding sibling was found. For schizophrenics, the sibling preceding the patient was of the opposite sex for 68 percent and 71 percent of male and female patients, respectively. The converse pattern was observed among the control subjects. The etiological significance of this finding is discussed. (17 references)—Journal abstract, modified.

4477. Cancro, R. (Department of Psychiatry, New York University Medical Center, 550 First Ave., New York, NY 10016) The schizophrenic syndrome: Its dubious past and its certain future. Hillside Journal of Clinical Psychiatry, 1(1):39–56, 1979.

The history and future of schizophrenia are discussed. It is contended that it is essential to identify the assumptions underlying any conceptualization of the schizophrenic syndrome before proceeding to develop diagnostic criteria. Various goals and methods of treatment are discussed. It is concluded that schizophrenias be thought of as biological disorders having both genetic and environmental components in their origin. (17 references)

4478. Glaister, J.; Feldstein, S.; and Pollack, H. (Clarke Institute of Psychiatry, 250 College Street, Toronto, Ontario M5T IR8, Canada) Chronographic speech patterns of acutely psychotic patients: A preliminary note. Journal of Nervous and Mental Disease, 168(4):219–223, 1980.

The likelihood that amount of vocal activity reflects degree of psychopathology and change with treatment in psychiatric patients was investigated by analyzing the chronographic speech patterns in five acute schizophrenics. After interviews, the Brief Psychiatric Rating Scale was used to rate the extent of the patient's pathology. In addition, the patient and interviewer separately completed a questionnaire to elicit their perceptions of the interview. Relative amounts of patient vocal activity were negatively related to interviewer ratings of general level of psychopathology and to several aspects of perceptions of the interview. The number of interviews per patient, however, was too few to permit evaluation of treatment effects. (16 references)—Author abstract, modified.

4479. Hermann, I. (Child Guidance Centre, 3 Spring Garden Lane, Gosport, Hampshire, England) Some aspects of psychotic regression. A Schreber study. International Review of Psycho-Analysis, 7 (Part 1):2–10, 1980.

The autobiography of Paul Schreber (1903), which describes the paranoid schizophrenia from which Schreber suffered, is reviewed, and the manifestations of psychotic regression noted by Schreber are discussed. It is suggested that the regression that takes place in Schreber is a regression into the infantile clinging/ongoing in search state. In terms of the ego, it is a regression to primitive perceptions; in terms of the superego, it is a regression to childhood emotions elicited by a forceful teacher/father image. Schreber's enthusiasm for music is interpreted as a force driving the sexual instincts towards regression. (30 references)—Author abstract, modified.

4480. LaTorre, R.A., and Piper, W.E. (Department of Psychology, University of British Columbia, 2075 Wesbrook Mall, Vancouver, British Columbia, Canada V6T 1W5) Gender identity and gender role in schizophrenia. Journal of Abnormal Psychology, 88(1):68–72, 1979.

The Bem Sex-Role Inventory, the Role Preference Test, the Embedded Figures Test (EFT), and the MMPI were given to 22 recently admitted individuals with affective disorders, 23 recently admitted schizophrenics, 21 long-term schizophrenics, and 21 noninstitutionalized controls in a study of gender identity. All groups demonstrated intact gender identity and gender role adoption as measured by the EFT and the MMPI masculinity and femininity scales, respectively. The two schizophrenic groups, in contrast with the two control groups, demonstrated a confused gender role adoption, as measured by the Bem Sex-Role Inventory; and they tended to choose more opposite-sex roles on the Role Preference Test. Length of hospitalization correlated with Role Preference Test scores, but only for females. Multiple administration of the Bem inventory revealed that all groups were aware of differences in gender roles; all groups noted that their parents would have been more pleased had they adopted sex-appropriate gender roles. Noninstitutionalized controls and recently admitted schizophrenics believed the ideal patient was significantly more feminine than masculine; long-term schizophrenics and those with affective disorders possessed a knowledge more typical of females than of males. (9 references)—Author abstract, modified.

4481. Matthews, W.C. (No address given) Effects of a work activity program on the self concept of chronic schizophrenics. Dissertation Abstracts International, 41(1):358–B, 1980.

The effects of involvement in a work activity program on the self-esteem and selected personal and social behaviors of 25 chronic schizophrenic ex-patients residing in a large board and care home in Southern California were investigated. The 25 experimental subjects were matched with 25 control subjects living in the same facility on diagnosis of chronic schizophrenia, intelligence, years of education, and age. Subjects were tested individually on the Tennessee Self Concept Scale (TSCS), the vocabulary subtest of the Wechsler Adult Intelligence Scale (WAIS), and their progress toward rehabilitation using the Staff Evaluation Scale. Ten weeks later all subjects were retested on the TSCS and the Staff Evaluation Scale. Subjects who participated in the work experience were found to increase their levels of self-esteem significantly over the 10-week period, while control subjects did not. Number of deviant signs subscale of the TSCS was found to discriminate the experimental group from the control group on both pretest and posttest administrations. In addition, the experimental group was found to have significantly decreased their scores on this subscale over the 10-week program period.—Journal abstract, modified.

4482. Palframan, D.S. (Children's Psychiatric Out-Patient Department, Royal Ottawa Hospital, Ottawa, Ontario, Canada) Two shootings. Canadian Journal of Psychiatry, 24(1):61–64, 1979.

Two case reports of murders involving men who were later found not guilty by reason of insanity are presented. Both men suffered from paranoid delusions. The ways in which paranoid states can result in violence are illustrated. One case shows a more classical pattern of paranoia associated with immigration, symptomatic use of alcohol, homosexual fears, and schizophrenic thought disorder, while the other case did not involve alcoholism or schizophrenia. The role of forensic psychiatrists in such cases and the dilemmas they face in determining criminal intent are examined. (9 references)

4483. Rosser, R. (Department of Psychiatry, Charing Cross Hospital Medical School, University of London, Fulham Palace Road, London W6 8RF, England) The psychopathology of feeling and thinking in a schizophrenic. International Journal of Psycho-Analysis, 60(Part 2):177–188, 1979.

Brief analytic psychotherapy with a 22-year-old schizophrenic who was treated twice weekly for 10 months and then followed up for 2 years is described. During therapy, reintegration occurred in the patient's affective and cognitive processes. Despite his subjective experience of loss of the capacity for thought and for verbal and nonverbal communication, he had an unusual ability for conveying the stages by which he moved from total confusion and thought disorder to normal intellectual functioning, and for understanding the connections between his various experiences. Four phases of therapy are defined: a phase of disintegration and undifferentiation lasting 6 weeks, a phase of depression lasting 5 weeks, a phase of multiple feelings lasting 14 weeks, and a phase of self-sustained development, starting in the 25th week and continuing beyond the end of therapy. The patient identified two major types of divisions between thinking, feeling, and acting parts of himself and between masculine and feminine parts. Insight into these divisions helped him to understand disorders in his perception of time, and in thinking, remembering, and using words and other symbols. (15 references)—Author abstract, modified.

4484. Watson, C.G., and Jacobs, L. (Research Service, Veterans Administration Medical Center, St. Cloud, MN 56301) Interrelationships and correlates of four measures of pleasure deficit. Journal of Clinical Psychology, 36(1):142–147, 1980.

Four measures currently used to assess pathological deficit in the ability to experience pleasure were compared using 56 schizophrenic inpatients as subjects. The Watson Anhedonia Interview scale was found to be less reliable than the others, but was correlated as often with measures of pleasure seeking as they were after correction for attenuation. The Chapman, Chapman, and Raulin Social and Physical Anhedonia scales demonstrated superior reliability and more correlations with pleasure-seeking ratings than the other scales. However, their relatively modest relationships with measures of psychopathology suggested that the pleasure deficits they measure best may not be as characteristic of psychiatric conditions as that reflected by the Anhedonia Interview. It is reported that the Zuckerman General Sensation Seeking scale showed less reliability than the Chapman scales and fewer correlations with both pleasure seeking and psychopathology than the others. (14 references)—Author abstract, modified.

Diagnosis

4485. Chelune, G.J.; Heaton, R.K.; Lehman, R.A.W.; and

Robinson, A. (Department of Psychology, University of Georgia, Athens, GA 30602) Level versus pattern of neuropsychological performance among schizophrenic and diffusely brain-damaged patients. Journal of Consulting and Clinical Psychology, 47(1):155–163, 1979.

Differences in both mean level and pattern of neuropsychological test performance were examined among groups of acute schizophrenic and diffusely brain-damaged patients. The Wechsler Adult Intelligence Scale (WAIS) subtests and the 12 average impairment rating (AIR) variables derived from the Halstead-Reitan Neuropsychological Test Battery were administered. The schizophrenics performed at a significantly higher level than the brain-damaged patients on both test batteries. Discriminant function analyses were used to estimate the diagnostic utility of level versus pattern of performance on the WAIS and AIR in discriminating the schizophrenics from the brain-damaged patients. The results suggest that mean level of performance can be used to discriminate clearly defined schizophrenic and diffusely brain-damaged groups, but that pattern analysis offers little additional information. (34 references)—Author abstract, modified.

4486. Gharagozlou, H., and Behin, M.T. (Neuropsychiatric Department, Pahlavi University, Shiraz, Iran) Diagnostic evaluation of Schneider first rank symptoms of schizophrenia among three groups of Iranians. Comprehensive Psychiatry, 20(3):242–245, 1979.

Results of a validity study of Schneider first rank symptoms for schizophrenia among Iranians are briefly reviewed. The findings indicate that the Schneider diagnostic procedure is valid, but that the symptoms are not pathognomic, as they are seen with considerable frequency in other mentally ill persons. The test can best be used to confirm the diagnosis of schizophrenia. (6 references)

4487. Perzynski, J. (Klinika Psychiatryczna AM, ul. Abramowicka, 20–442 Lublin, Poland) Difficulties in diagnosing the onset of schizophrenia when accompanied by neurotic disorders. Psychiatria Polska, 13(1):57–62, 1979.

Difficulties of diagnosing schizophrenia in its initial stage, when it is accompanied by neurotic disorders, are discussed. The problem is particularly important because early biological treatment of schizophrenia is reportedly giving good results, and the rate of full remission in cases of patients treated in the first year of illness is twice as high as that in patients who received no treatment. However, diagnosis is difficult when the onset of schizophrenia is concealed by characterological changes (particularly during puberty), by anomalies of sexual impulse, or by a neurotic disorder. (51 references)

4488. Taylor, M.A. (Department of Psychiatry and Behavioral Sciences, Chicago Medical School, North Chicago, IL 60064) Brain norepinephrine and dopamine in schizophrenia. Science, 204 (4388):94, 1979.

A comment is presented on the work by Farley (1978) on the norepinephrine patterns in four patients diagnosed as paranoid schizophrenics. It is suggested that this work was a clinical anachronism. Diagnosis made by Bleuler's criteria was without a statement of reliability or validity. Without use of one of several sets of modern research criteria, the findings are a non sequitur of hard data. (2 references)

Genetics

4489. Cancro, R. (Department of Psychiatry, New York University Medical Center, New York, NY 10016) The clinical relevance of genetic studies in schizophrenia. Psychiatric Annals, 9(1):103–107, 111, 1979.

A series of articles on genetic research in schizophrenia, which were printed in the January 1979 issue of *Psychiatric Annals*, are reviewed. The history of the conceptualization of schizophrenia as a specific disorder, or group of disorders, is reviewed. A syndrome conceptualization of the schizophrenias is indicated as the best means of dealing with the absence of independently valid criteria for diagnosis. The problems of diagnosis are secondary to those of etiology. It is known that both genetic and environmental factors operate in the etiology of the disorder. Although research has revealed some of the necessary conditions for the emergence of the syndrome, those conditions sufficient to guarantee its emergence have not been identified. It is concluded that the treatment of schizophrenia is empiric—the treatment that works in one person will be harmful in a second and have no effect in a third. (10 references)

4490. Gottesman, I.I. (Behavioral Genetics Center, University of Minnesota, Minneapolis, MN 55455) Schizophrenia and genetics: Toward understanding uncertainty. Psychiatric Annals, 9(1):54–57, 61, 64–65, 68–69, 73, 77–78, 1979.

Recent research on the etiology of schizophrenia is reviewed. The findings of Danish studies of the incidence of schizophrenia among children of schizophrenics who had been adopted by normal parents are discussed. A series of tenets, drawn from the various findings of research projects, are presented to aid in the understanding and interpretation of the diverse, and sometimes unreplicated, etiological evidence. These tenets include: no environmental causes have been found which will produce schizophrenia in persons unrelated to a person with schizophrenia; schizophrenia occurs in both industrialized and undeveloped countries; there is a marked social class gradient in the prevalence of schizophrenia within large urban communities; the risk of schizophrenia to relatives of index cases increases markedly with degree of genetic relatedness; children of schizophrenics adopted at an early age develop schizophrenia at rates almost as high as those children raised by their affected parents; children of normal parents who are adopted into homes where a parental figure becomes schizophrenic do not show an increased rate of schizophrenia; and the risk to relatives of schizophrenics varies with the severity of the illness in the proband, the number of relatives already affected, and the status of the other parent. (35 references)

4491. Nicol, S.E., and Heston, L.L. (St. Paul Ramsey Medical Center, University of Minnesota, Minneapolis, MN 55455) The future of genetic research in schizophrenia. Psychiatric Annals, 9(1): 32–33, 36–37, 41–43, 46–49, 53, 1979.

The problems which face research into the genetic transmission of schizophrenia are discussed. Although research indicates that there is a greater incidence of schizophrenia among relatives of schizophrenics than there is in the general population, investigators have yet to identify a definite trait that reliably can be said to be present or absent in probands and relatives. Biochemical attempts to explain the possibilities of genetic transmission of schizophrenia are reviewed. The principles of neuronal function and hormonal action are discussed, with particular emphasis on the possible role of dopamine in schizophrenia. Although the possibilities for causality in schizophrenia are complex, specific patterns are emerging. Knowledge about biochemical systems has expanded rapidly in the past two decades, and the ways that genes interact with the environment to produce the schizophrenic phenotype may be understood in the near future. (30 references)

4492. Welner, A.; Welner, Z.; and Fishman, R. Department of Psychiatry, Washington University School of Medicine, 4940 Audubon Avenue, St. Louis, MO 63110) The group of schizoaffective and related psychoses: IV. A family study. Comprehensive Psychiatry, 20(1):21–26, 1979.

Families of schizoaffective probands were studied in the hope that the diagnosis in the sick first-degree family members would help determine which diagnosis or diagnoses are associated with schizoaffective illness. The 114 probands had 619 relatives, of which 551 were located. Fifty-three families agreed to participate, and of those, 20 families were chosen because each had one or more relatives with a history or presence of affective or psychotic symptoms. Psychiatric symptoms in the relatives are charted, and the course of illness is reported. It is shown that sick first-degree relatives manifest a very similar clinical picture, course, and outcome as the probands. Since the course of illness in both probands and relatives was chronic, psychotic, and deteriorating, the characteristics were of schizophrenia and not of affective disorder. Neither the presence of numerous affective symptoms, nor the family study indicated the presence of schizoaffective psychosis as a diagnostic entity. It is suggested that the term undiagnosed rather than schizoaffective psychosis be used when encountering acute cases of psychotic and affective symptoms. (26 references)—Author abstract, modified.

High-Risk Studies

4493. Erlenmeyer-Kimling, L.; Cornblatt, B.; and Fleiss, J. (New York State Psychiatric Institute, New York, NY 10032) High-risk research in schizophrenia. Psychiatric Annals, 9(1):79–80, 85–87, 90–91, 94–99, 102, 1979.

A prospective longitudinal study of individuals at high statistical risk for schizophrenia is described. Two hundred and five children between the ages of 7 and 12 years old were observed for 7 years. Of these children, 67 had one schizophrenic parent, 13 had two schizophrenic parents, 25 had a parent with some psychiatric disorder not related to schizophrenia, and 100 had parents who had never been treated for any psychiatric disorder. Data were gathered through structured interviews, blood samples, the MMPI, the Continuous Performance Test, the Bender Gestalt Test, the Draw a Person Test, the Lincoln Oretsky Test of Motor Impairment, and scaled ratings of videotaped behavior. The study appears to have identified a subgroup of high-risk children who show cognitive (attentional) deficits, some degree of maturational lag on neuropsychological functions, and early behavioral deviations that are sufficiently severe to warrant hospitalization or psychiatric treatment. (19 references)

4494. Wynne, L.C. (Department of Psychiatry, University of Rochester, Rochester, NY 14642) Risk-reducing factors for schizophrenia. Psychiatric Opinion, 16(2):2, 1979.

Health enhancing factors in individuals at high risk for schizophrenia and other psychiatric illnesses are discussed within the context of initial results of a study of high-risk offspring. It is suggested that rather than the traditional pathology oriented psychiatric research preoccupation, research into factors associated with healthy mental functioning of high-risk individuals might prove rewarding. One study of offspring in 145 study families with one parent with a history of psychiatric hospitalization suggests that severely deviant communications of one spouse may be counteracted by an active, nondeviant, presumably corrective spouse. Additional studies related to attempts to shorten hospital stays suggest the importance of adequate family and community support systems. (3 references)

Prognosis

4495. Johnstone, E.C.; Frith, C.D.; Gold, A.; and Stevens, M. (Department of Psychiatry, Northwick Park Hospital and Clinical Research Centre, Watford Road, Harrow, Middlesex, HA1 3UJ, England) The outcome of severe acute schizophrenic illnesses after one year. British Journal of Psychiatry, 134 (January):28–33, 1979.

The relevance for outcome of clinical, social, and psychological variables present at the onset of an acute schizophrenic illness were examined in terms of social functioning and persistent psychotic features at 1 year. Forty-five patients defined by Present State Examination (PSE) criteria were assessed in clinical, cognitive, and social terms before being entered in a 4-week study of the isomers of flupenthizol and placebo. At the end of 1 year, they were reassessed in the same terms. The clinical and psychological features of the acute illness and the drug treatment given did not predict outcome. It is reported that poor outcome in social terms was significantly related to severe social isolation in the initial assessment and to the presence of nuclear symptoms and negative schizophrenic features at followup. (20 references)—Author abstract, modified.

4496. Knight, R.A.; Roff, J.D.; Barrnett, J.; and Moss, J.L. (Department of Psychology, Brandeis University, Waltham, MA 02154) Concurrent and predictive validity of thought disorder and affectivity: A 22-year follow-up of acute schizophrenics. Journal of Abnormal Psychology, 88(1):1–12, 1979.

Fifty-one male patients with hospital diagnoses of schizophrenia in the military service were followed up through Veterans Administration hospital records 22 years after their initial service hospitalization in a study of the predictive validity of thought disorder and affectivity. Results reveal that severity of thought disorder did not predict outcome, but measures of affectivity and interpersonal competence did so with high significance. An attempt is made to explain why affectivity has received so little attention in the research literature. It is suggested that recent research diagnostic criteria for schizophrenia are inadequate, because the criteria focus almost exclusively on the less predictive symptoms of disordered thought and exclude assessment of affectivity and interpersonal competence. (33 references)—Author abstract.

4497. Newmark, C.S.; Konanc, J.T.; Simpson, M.; Boren, R.B.; and Prillaman, K. (Department of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, NC 27514) Predictive validity of the Rorschach Prognostic Rating Scale with schizophrenic patients. Journal of Nervous and Mental Disease, 167(3):135–143, 1979.

The prognostic validity of the Klopfer's Prognostic Rating Scale (PRS), an instrument using responses to Rorschach cards, was assessed with 98 schizophrenic patients. Through the use of a standardized structured interview and a diagnostic system for schizophrenia based on the use of discriminant function analysis with nonpathognomonic symptom combinations, a reliable and valid system was developed to establish the criterion diagnosis. Results confirm the practical utility of the PRS with schizophrenic patients; efficient prediction was obtained when other relevant demographic and nontest variables were controlled. Further, the concept of ego strength from which the PRS was developed does not appear to be too global a characteristic when the area for change is specifically delinated. (86 references)—Author abstract, modified.

Psychiatry and the Law

4498. Soloff, P.H.; Jewell, S.; and Roth, L.H. (Department of Psychiatry, University of Pittsburgh, Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15261) Civil commitment and the rights of the unborn. American Journal of Psychiatry, 136(1):114–115, 1979.

Clinical management of the pregnant psychotic patient is discussed, presenting a case report in which civil commitment of the mother for the duration of pregnancy was used. Commitment was granted to afford protection to the unborn child over the protest of the mother. The court therefore upheld the welfare of the unborn as if it were already a person in being, with rights to protection under the broad principle of *parens patriae*. (8 references)

Psychological Theory

4499. Salonen, S. (Purokatu 3, SF-20810 Turku 81, Finland) On the metapsychology of schizophrenia. International Journal of Psycho-Analysis, 60(1):73–81, 1979.

Schizophrenic fragmentation is considered from a drive/economic and structural point of view, starting from Freud's prestructural conceptions and Jacobson's metapsychological formulations. The central psychological mechanism in the schizophrenic disorder is a drive/energic decathexis of the basic psychic tissue, or the primal representative matrix, which has far-reaching consequences within the entire psychic organization. It is concluded that its influences naturally also extend to the realm of the more advanced psychic functions and macrostructures and will invalidate in a radical way the person's drive economy. (15 references)

Treatment

4500. Alexopoulos, G.S. (Department of Psychiatry, New York Hospital-Cornell University Medical Center, 21 Bloomingdale Road, White Plains, NY 10605) Lack of complaints in schizophrenics with tardive dyskinesia. Journal of Nervous and Mental Disease, 167(2):125–127, 1979.

The question of what proportion of patients with tardive dyskinesia do not complain about their symptoms was studied, as well as the reasons behind it. Eighteen of a population of 518 outpatients were found to fulfill diagnostic criteria for tardive dyskinesia. None of these patients complained to their therapists of their symptoms, and eight of them were not even aware of them. Five of the unaware patients were actively delusional or hallucinating. Since all 18 were chronic schizophrenics on neuroleptics, it is suggested that this group may not report their symptoms. The importance of these findings is emphasized since early diagnosis of tardive dyskinesia allows more chance for satisfactory intervention. (10 references)—Author abstract, modified.

4501. Chouinard, G.; Annable, L.; Ross-Chouinard, A.; and Kropsky, M.L. (Allan Memorial Institute, 1025 Pine Avenue West, Montreal, Quebec H3A 1A1, Canada) Ethopropazine and benztropine in neuroleptic-induced parkinsonism. Journal of Clinical Psychiatry, 40(3): 147–152, 1979.

A 12-week controlled study, in which ethopropazine was compared to benztropine in the treatment of parkinsonism induced by fluphenazine enanthate in 60 schizophrenic outpatients, is described. Ethopropazine and benztropine were found to be equally effective in controlling parkinsonian symptoms and were as efficacious as procyclidine, their previous antiparkinsonian drug. However, benztropine-treated patients had a significant increase in tardive dyskinesia compared to their condition during procyclidine treatment, and significantly more anxiety and depression than ethopropazine-treated patients. This suggests that benztropine is not the anticholinergic drug of choice in the treatment of neuroleptic induced parkinsonian symptoms, because of its more toxic central and peripheral atropinic effect. (13 references)—Author abstract.

4502. Chouinard, G.; Annable, L.; Ross-Chouinard, A.; and Nestoros, J.N. (Department of Psychiatry, McGill University, Montreal, Quebec, Canada) Factors related to tardive dyskinesia. American Journal of Psychiatry, 136(1):79–83, 1979.

The incidence of tardive dyskinesia among 261 schizophrenic outpatients treated with neuroleptics was investigated. A 31 percent incidence was found, and multiple linear logistic regressional analysis revealed a higher incidence among elderly patients, those with longer records of hospitalization, those for whom neuroleptic medication had little therapeutic effect, and those treated with fluphenazine. Patients manifesting tardive dyskinesia had fewer parkinsonian symptoms than those without the disorder, especially when tremors and akathisia were excluded from consideration. Multiple linear regression analysis revealed that brain-damaged patients and male patients were more susceptible to severe forms of the disorder, even though these factors were not implicated in its initial appearance. (16 references)—Author abstract, modified.

4503. Chouinard, G.; de Montigny, C.; and Annable, L. (Department of Psychiatry, McGill University, Montreal, Quebec, Canada) Tardive dyskinesia and antiparkinsonian medication. American Journal of Psychiatry, 136(2):228–229, 1979.

The effects of administration and subsequent withdrawal of the central anticholinergic agent procyclidine HCl in extrapyramidal symptoms were examined in 20 schizophrenic patients with significant tardive dyskinesia. Procyclidine had an effect on tardive dyskinesia opposite to that on parkinsonism, improving the latter but exacerbating the dyskinetic movements. Findings are consistent with the dopamine supersensitivity hypothesis of tardive dyskinesia—procyclidine may have exacerbated dyskinetic symptoms by its dopamine reuptake blocking property and/or its central anticholinergic activity. (10 references)

4504. Claghorn, J.L.; Mathew, R.J.; and Mirabi, M. (1300 Moursund Avenue, Houston, TX 77030) Penfluridol: A long acting oral antipsychotic drug. Journal of Clinical Psychiatry, 40(2):107–109, 1979.

In a 52-week double-blind study, once-weekly doses of penfluridol, a diphenylbutylpiperdine derivative with a half-life of 66 hours, were compared with once-daily doses of chlorpromazine in 56 schizophrenic outpatients receiving maintenance treatment. Both drugs were similarly effective in the control of psychotic symptoms over an extended period of time. While no major side effects occurred with either drug, central nervous system effects were reported by 21 penfluridol and 9 chlorpromazine subjects. Advantages of once-weekly doses are noted. (3 references)—Author abstract, modified

4505. Donlon, P.T.; Hopkin, J.; Schaffer, C.B.; and Amsterdam, E. (Department of Psychiatry, School of Medicine, University of California, Davis, 3340 V Street, Sacramento, CA 95817) Cardiovascular safety of rapid treatment with intramuscular haloperidol. American Journal of Psychiatry, 136(2):233–234, 1979.

The effects of rapid treatment of schizophrenia with intramuscular haloperidol on heartrate and blood pressure were investigated in 25 acutely psychotic patients whose mean age was 25 years. During the 6-hour study period, the total dose administered was 22.5 mg—range 10 mg to 40 mg. Analysis of variance indicated that there were no significant reductions in mean values for blood pressure and heartrate—both decreased gradually within the normal range. Only one patient showed a clinically significant decrease in blood pressure, which returned to pretreatment levels approximately 6 hours after initial injection. Results indicate a high degree of cardiovascular safety of intramuscular administration of haloperidol to healthy patients who require moderate treatment doses at 30-minute intervals. Risk may be greater in elderly and/or medically ill patients. (6 references)

4506. Donlon, P.T.; Hopkin, J.; and Tupin, J.P. (Dept. of Psychiatry, University of California,

School of Medicine, 3340 V St., Sacramento, CA 95817) Overview: Efficacy and safety of the rapid neuroleptization method with injectable haloperidol. American Journal of Psychiatry, 136(3): 273–278, 1979.

The literature on the rapid neuroleptization (titration) method with i.m. haloperidol is reviewed, and recommendations are made for further research to establish clearly the effectiveness and safety of this method of neuroleptic administration. Most of the approximately 650 predominantly schizophrenic and manic patients represented in the studies calmed down rapidly on medication, and some demonstrated an early reduction in core psychotic symptoms. The medication seems to have been well tolerated in all cases, with no reported major complications. It is concluded that the method shows definite merit with agitated and belligerent patients. (20 references)—Author abstract, modified.

4507. Echols, S.W. (California School of Professional Psychology, Berkeley 94704) A therapeutic milieu for treatment of schizophrenia: Development and change. Dissertation Abstracts International, 40(7):3388–B, 1980.

The history of Passage Way, an innovative milieu setting for treating schizophrenia, is presented from the point of view of 17 staff members. At various times and in different degrees, Passage Way has identified itself as a Laingian facility, a community agency, and a provider of traditional intensive psychotherapy of schizophrenia. During its history, Passage Way moved through three eras involving: (1) The charismatic affirmation of natural processes and the merger of personal and interpersonal concerns; (2) conflict over the change of charismatic expectations into status quo expectations, the tyranny of "process," and the overwhelming of staff's personal needs by the interpersonal; and (3) resolve, bringing new definitions and balancing of structure and process—personal and interpersonal. Passage Way history replicates change over time in psychotherapy of schizophrenia, milieu treatment, and Laingian facilities.—Journal abstract, modified.

4508. Escobar, J.I., and Tuason, V.B. (University of Tennessee, Memphis, TN 38163) Neuroleptic withdrawal dyskinesia. Psychopharmacology Bulletin, 15(2):71–74, 1979.

In a summary of a paper presented at the Annual Meeting of the New Clinical Drug Evaluation Units of the National Institute of Mental Health (NIMH), held in Key Biscayne, FL, May 1978, a study of neuroleptic withdrawal dyskinesia is described. Longitudinal observations were made using the Abnormal Involuntary Movement Scale (AIMS) on a cohort of 16 schizophrenic patients in which dyskinetic movements reappeared following abrupt withdrawal of a neuroleptic they had taken for 1 year under controlled conditions. Differential dyskinetic profiles are reported for patients receiving oral fluphenazine and for those receiving fluphenazine decanoate, with a faster and more severe withdrawal dyskinesia being seen in the former group. (9 references)

4509. Gelenberg, A.J.; Doller, J.C.; Schooler, N.R.; Mieske, M.; Severe, J.; and Mandel, M.R. (Massachusetts General Hospital, Boston, MA 02114) Acute extrapyramidal reactions with fluphenazine hydrochloride and fluphenazine decanoate. American Journal of Psychiatry, 136(2):217–219, 1979.

In a four center collaborative study, extrapyramidal symptoms (EPS) of fluphenazine hydrochloride and fluphenazine decanoate were compared in 290 schizophrenic inpatients. Results failed to reveal significant differences between the oral and depot fluphenazine in the occurrence of akathisia or Parkinson's syndrome. In addition, no correlations were found between the occurrence of any of the signs of these two disorders and age, sex, race, history of EPS, or previous anti-Parkinsonian drug use. The use of benztropine was significantly related to the presence of EPS. Data indicate that akathisia and Parkinsonism are not serious problems during the first 7 weeks of treatment with either form of fluphenazine. (10 references)

4510. Horrobin, D.F. (Clinical Research Institue, 110 Pine Avenue West, Montreal H2W 1R7, Canada) Prostaglandin deficiency and endorphin excess in schizophrenia: The case for treatment with penicillin, zinc, and evening primrose oil. Journal of Orthomolecular Psychiatry, 8(1):13–19, 1979.

A unified approach to the pathogenesis and treatment of schizophrenia is described. Prostaglandin deficiency and endorphin excess are linked with the excess dopamine and orthomolecular hypotheses and viewed as different complementary aspects of schizophrenia's etiology. The endorphin and prostaglandin rationales for schizophrenia are briefly described, and the results of therapeutic trials of novel treatment of schizophrenia with penicillin, zinc, and evening primrose oil are reported. Partly because of its sound theoretical base and its freedom from side effects, treatment with penicillin, evening primrose oil, and zinc promises to be a major advance. Because this therapy is in the initial stages of experimentation, however, an optimal dose regime probably remains to be achieved. (20 references)

4511. Jus, A.; Jus, K.; and Fontaine, P. (Centre Hospitalier Robert Giffard, 2601 de la Canardiere, Beauport, Quebec G1J 2G3, Canada) Long term treatment of tardive dyskinesia. Journal of Clinical Psychiatry, 40(2):72–77, 1979.

A 4-year trial to treat tardive dyskinesia by a very slow progressive stepwise diminution of the neuroleptic dose and of the antiparkinsonian agent, as well as by administration of small slowly increasing and then decreasing doses of reserpine or haloperidol, was conducted in a sample of 62 chronic schizophrenic patients. This treatment program resulted in the disappearance of tardive dyskinesia in 23 patients and improvement in 26 patients, and had no effect in 13 patients. The group of patients with disappearance of tardive dyskinesia had a mean age significantly lower than the other groups. The rationale of this treatment was based on the concept of desensitization by a slow progressive unblocking of dopaminergic receptor sites. The rabbit syndrome, another tardive neuroleptic side effect, was successfully treated in an additional seven patients by antiparkinsonian drugs. (25 references)—Author abstract.

4512. Kane, J., and Di Scipio, W.J. (South Beach Psychiatric Center, 777 Seaview Avenue, Staten Island, NY 10305) Acupuncture treatment of schizophrenia: Report on three cases. American Journal of Psychiatry, 136(3): 297–302, 1979.

A 9-week blind, controlled study of the effects of acupuncture on schizophrenic illness in three patients on an inpatient ward of a psychiatric hospital is described. The effects of acupuncture, pseudoacupuncture (random needling), and nontreatment control periods were compared in a design in which subjects served as their own controls. Two patients who had had florid schizophrenic symptoms responded positively to true acupuncture and negatively to pseudoacupuncture. The third patient, whose symptoms were primarily affective/depressive, showed no significant response to treatment. Mechanisms thought to be involved in the etiology of schizophrenia, including the cortical arousal hypothesis, are explored. (16 references)—Author abstract, modified.

4513. Kane, J.; Rifkin, A.; and Quitkin, F. (Long Island Jewish-Hillside Medical Center, New York, NY 10001) A pilot study of "low-dose" fluphenazine decanoate in outpatient schizophrenics. Psychopharmacology Bulletin, 15(2):78–80, 1979.

In a summary of a paper presented at the Annual Meeting of the New Clinical Drug Evaluation Units of the National Institute of Mental Health (NIMH), held in Key Biscayne, FL, May 1978, a pilot study of low-dose fluphenazine decanoate in therapy for outpatient schizophrenics is described. Fifty-seven outpatients meeting research diagnostic criteria for schizophrenia and in remission for at least 4 weeks or at a stable clinical plateau were openly switched from standard doses of fluphenazine decanoate to doses between 1.25 mg and 5 mg i.m., every 2 weeks (each patient received one tenth of his previous dosage). Results suggest that low-dose maintenance treatment may be adequate for prophylaxis in some patients, and that those who relapse may respond well to brief periods of higher dosage without significant disruption in their lives or need for rehospitalization. (9 references)

4514. Korsgaard, S., and Skausig, O.B. (Department of Psychiatry, Municipal Hospital, Oster Farimagsgade, 3, DK-1399, Copenhagen K, Denmark) Increase in weight after treatment with depot neuroleptics. Acta Psychiatrica Scandinavica, 59(2):139–144, 1979.

A drug trial was performed to investigate weight changes in 99 schizophrenic female patients who were treated with clopenthixol decanoate or perphenazine enanthate after prior treatment with different oral neuroleptics. A significantly higher mean weight after the oral treatment period was found and a slight, but not statistically significant, further weight increase after the following depot period. In addition, the rate of increase in weight was significantly lower during the depot treatment period. These increases might have been due to achievement of a steady state in weight during the first treatment period with oral intake. No difference was found between clopenthixol decanoate and perphenazine enanthate as regards change in weight or rate of change in weight. (8 references)—Author abstract.

4515. Matulay, K. (Klinika Psychiatryczna Wydzialu Lekarskiego, Martin, Czechoslovakia) Rehabilitation in schizophrenia. Psychiatria Polska, 13(1):47–52, 1979.

Principles of rehabilitation of schizophrenics and trends of rehabilitation therapy in various countries are discussed. In Czechoslovakia, emphasis was put for 40 years on physical work, sports, and musical therapy using the method of group therapy. Social rehabilitation has been emphasized in recent years. It is concluded that rehabilitation of schizophrenics is a complicated medical, social, and economic problem. Rehabilitation and psychotherapy are closely related. Rehabilitation in schizophrenia is very important socially and economically, because schizophrenia causes disability of young people, and as much as 1 percent of the population is threatened by it. Timely rehabilitation may prevent the chronic stage of schizophrenia.

4516. Miller, H.R., and Dermer, S.W. (Social and Vocational Rehabilitation Unit, Hamilton Psychiatric Hospital, Hamilton, Ontario, Canada L8N 3K7) Quasi-experimental follow-up of token-economy and conventional treatment graduates. Journal of Consulting and Clinical Psychology, 47(3):625–627, 1979.

A conventional treatment program included in a token economy designed to prepare patients for community living was evaluated. The mean number of days spent in hospital per month, over a 30-month period, for a group of young chronic schizophrenics was reduced as compared to pretreatment data. The slope of these data also changed from a positively increasing one before treatment to zero after treatment. A group of similar, although not directly comparable, chronic schizophrenics showed no change in either level of slope of these data after completing a conventional treatment program alone. These results suggest that token economies may enhance conventional treatment techniques, and that they may be useful in preparing patients for community living if attempts are made to include factors that encourage response generalization. (3 references)—Author abstract, modified.

4517. Otteson, J.P. (Dept. of Psychology, University of Santa Clara, Santa Clara, CA 95053) Curative caring: The use of buddy groups with chronic schizophrenics. Journal of Consulting and Clinical Psychology, 47(3):649–651, 1979.

The utility of altruism as a basis for group therapy treatment of long-term schizophrenic patients was investigated. Thirty-six chronic patients were assigned to one of three group conditions: an altruistic (buddy oriented) group, a traditional (self-oriented) group, or a no treatment control group. Outcome results after 6 weeks of therapy suggest that the altruistic group (which focused each member's attention on the facilitation of his buddy's discharge from the hospital) was more effective than the self-oriented or no treatment groups, as measured by discharge and recidivism rates. (5 references)—Author abstract, modified.

4518. Prusoff, B.A.; Williams, D.H.; Weissman, M.M.; and Astrachan, B.M. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06520) A controlled clinical trial of amitriptyline added to perphenazine in the treatment of depressed schizophrenics. Psychopharmacology Bulletin, 15(2):80–81, 1979.

In a summary of a paper presented at the Annual Meeting of the New Clinical Drug Evaluation Units of the National Institute of Mental Health (NIMH), held in Key Biscayne, FL, May 1978, a controlled clinical trial of amitriptyline added to perphenazine in the treatment of depressed schizophrenics is described. Results of a double-blind, randomized, placebo-controlled clinical trial, designed to evaluate the combination of perphenazine and amitriptyline with that of perphenazine alone in the treatment of 35 ambulatory chronic schizophrenic patients with depressive symptoms, indicate that the addition of amitriptyline to perphenazine was effective in reducing depressive symptoms on the Raskin Depression Scale at 4 months of treatment. However, patients receiving amitriptyline reported more thought disorders. (14 references)

4519. Rifkin, A.; Quitkin, F.; Kane, J.; Klein, D.F.; and Ross, D. (College of Physicians and Surgeons, Columbia University, New York, NY 10032) The effect of fluphenazine upon social and vocational functioning in remitted schizophrenics. Biological Psychiatry, 14(3):499–508, 1979.

Thirty-six remitted schizophrenics who participated in an outpatient study of fluphenazine decanoate or oral fluphenazine versus placebo given for a year were examined for the effect of drug treatment upon social and vocational functioning. Only the period before any clinical relapse was evaluated. No difference was found between those on drug or placebo. It is concluded that antipsychotic drugs, at least in the context of an aftercare clinic offering a rich spectrum of nonpharmacological services, and when combined with antiparkinson medication, do not interfere with social and vocational functioning. (15 references)—Author abstract.

4520. Satten, N.R., and Singer, M. (Institute of the Pennsylvania Hospital, Philadelphia, PA 19107) Successful treatment in a woman with Down's syndrome. Psychiatric Opinion, 16(1):36–40, 1979.

The successful treatment of a case of propfschizophrenia (schizophrenia grafted upon mental retardation) in a young woman with Down's syndrome is described. The literature on the condition is surveyed, and suggestions are offered to explain the unusual successful outcome of this case. The usefulness of understanding and utilizing individual and family dynamic issues in the multidisciplinary treatment of the emotionally disturbed, mentally retarded patient is demonstrated. (17 references)—Author abstract.

4521. Schlosberg, A., and Shadmi, M. (Beer Ya'acov Psychiatric Hospital, Tel Aviv University Sackler School of Medicine, Beer Ya'acov, Israel) A comparative controlled study of two long-acting phenothiazines: Pipotiazine palmitate and fluphenazine decanoate. Current Therapeutic Research, 23(5):642–654, 1978.

Seventy five hard-core chronic schizophrenics received at random, after a washout period, fluphenazine, pipotiazine, and placebo in a double-blind study. Initially, the medications were administered orally, and then the patients were given long-acting injections for each of 15 months. Finally, the group of improved patients was divided in half, receiving either placebo injections or continuing with their medication. Patients were evaluated with the Brief Psychiatric Rating Scale, the Nurses' Observation Scale for Inpatient Evaluation, global clinical evaluation, social functioning rating, and rating by patient's family. Two patients receiving placebo, nine patients receiving fluphenazine decanoate, and nine patients receiving pipotiazine palmitate showed improvement. Analysis of these results was undertaken to determine favorable relative indications of each psychoactive drug for the specific psychiatric population and illness involved. (16 references)—Author abstract, modified.

4522. Schooler, N.R.; Levine, J.; and Severe, J.B. (Psychopharmacology Research Branch, National Institute of Mental Health, Rockville, MD 20857) Depot fluphenazine in the prevention of relapse in schizophrenia: Evaluation of a treatment regimen. Psychopharmacology Bulletin, 15(2):44–47, 1979.

In a summary of a paper presented at the 16th Annual Meeting of the American College of Neuropsychopharmacology, held in San Juan, Puerto Rico, December 1977, a study of the relative effectiveness of oral medication and long-acting injectible phenothiazine in preventing relapse in schizophrenic patients newly discharged to the community is described. Two hundred fourteen schizophrenics who had been randomly assigned to fluphenazine decanoate or fluphenazine hydrochloride while floridly ill and hospitalized were seen every 3 weeks for double-blind drug administration for 1 year or until clinical relapse. No significant differences in rate of relapse were found between the two regimens.

4523. Schraa, J.K.; Lautmann, L.; Luzi, M.K.; and Screven, C.G.

(Department of Psychology, University of Wisconsin-Milwaukee, Milwakee, WI 53201) Establishment of nondelusional responses in a socially withdrawn chronic schizophrenic. Journal of Applied Behavior Analysis, 11(3):433–434, 1978.

Multiple treatment interventions including instructions, modeling, timeout, avoidance of repetition, and reinforcement were used to establish factual answers to personal background questions in a withdrawn and socially unresponsive chronic schizophrenic. A multiple baseline design across verbal replies demonstrated that the changes in behavior were brought about by the treatment interventions. Introduction of the experimental interventions produced an increase from a baseline level of zero to at least 80 percent correct for each of four questions. Maintenance was found to be complete at the 9- and 10-month followups, but at the 12-month followup interview, the subject answered one question incorrectly.—Author abstract, modified.

4524. Shopsin, B., and Klein, H. (Department of Psychiatry, Neuropsychopharmacology Research Section, New York University-Bellevue Hospital Center, New York, NY 10016) Clozapine: Double-blind control trial in the treatment of acute schizophrenia. Psychopharmacology Bulletin, 14(2):12–15, 1978.

Using a double-blind control design, the effects of clozapine and chlorpromazine in treatment of acute schizophrenia were compared. After a placebo washout period of 7 to 14 days, the patients were treated in a fixed dose buildup period of 7 days reaching a maximum of 300 mg clozapine or 600 mg chlorpromazine. This was followed by a 28-day flexible dosage period buildup to a maximum of 900 mg/day of clozapine or 1,800 mg/day chlorpromazine. Analyses indicate that clozapine is significantly better than placebo, and chlorpromazine is not consistent in showing improvement compared to the placebo group under all objective parameters measured. Clozapine showed a significant effect in ameliorating depressive symptoms as well, whereas, chlorpromazine had no effect on these symptoms. None of the patients receiving clozapine showed any indication of extrapyramidal symptoms. Several patients with tardive dyskinesia showed definite improvement under clozapine treatment. Findings suggest that best treatment results are achieved under clozapine conditions. (10 references)

4525. Sidorowicz, S.; Firko, M.; Wasik, A.; Szewczyk, Z.; Szepietowski, T.; and Weyde, W. (Psychiatric Clinic, Medical Academy, Kraszewskiego 25, Wroclaw, Poland) Clinical trial of hemodialysis in chronic schizophrenia. Acta Psychiatrica Scandinavica, 61(3):223–227, 1980.

A hemodialysis program was carried out in four male chronic schizophrenic patients, with clinical assessment of mental and physical state following each dialysis. Eleven to 20 dialyses were conducted either once a week (two patients) or twice a week (two patients). Neuroleptics were withdrawn. A short period of slight, unspecific improvement was followed by a deterioration in all cases. At the end of the dialysis program, none of the patients improved. It is recommended that further research be done on the efficacy of dialysis in chronic schizophrenia. (15 references)—Author abstract, modified.

4526. Simpson, G.M.; Lee, J.H.; Shrivastava, R.K.; and Branchey, M.H. (Rockland Research Institute, Orangeburg, NY 10962) Baclofen in the treatment of tardive dyskinesia and schizophrenia. Psychopharmacology Bulletin, 14(2):16–18, 1978.

The effect of baclofen in the treatment of tardive dyskinesia and schizophrenia was evaluated in chronic treatment-resistant schizophrenic patients (*n* = 12). Baclofen was administered for up to 7 weeks, and there was a 1-week placebo washout in only a few patients. All medication was administered on a b.i.d. basis, and the dose schedule ranged from 10 to 120 mg daily without any discernible improvement. In fact, the condition of 10 patients worsened dramatically over the trial. The only side effect which occurred during baclofen administration was an occasional mild tremor which did not appear to be dose related. Results suggest that baclofen is of no value in schizophrenia treatment. (4 references)

4527. Siris, S.G.; van Kammen, D.P.; and Docherty, J.P. (New York State Psychiatric Institute, 722 West 168th St. New York, NY 10032) Use of antidepressant drugs in schizophrenia. Archives of General Psychiatry, 35(11): 1368–1377, 1978.

The therapeutic efficacy of tricyclic antidepressants and monoamine oxidase inhibitors in schizophrenic patients is reviewed. In general, the use of these drugs alone was found not to be warranted in schizophrenia, except perhaps in the pseudoneurotic subgroup. In most cases, combinations of antidepressants and phenothiazines were no more beneficial than phenothiazines alone. In particular, the conditions of agitated patients and patients with histories of social deviance dating back to childhood were often made worse by the addition of an antidepressant. However, when the patients who demonstrated symptoms of clinical depression other than anergia were isolated from several of these studies, it was found that they constitute a subgroup that is often benefited by use of these combinations. Favorable and unfavorable clinical response patterns are discussed, and recommendations for future research are outlined. (175 references)—Author abstract, modified.

4528. Soskis, D.A. (Department of Psychiatry, 5–OPD, Temple University Health Sciences Center, 3401 North Broad St., Philadelphia, PA 19140) Schizophrenic and medical inpatients as informed drug consumers. Archives of General Psychiatry, 35(5):645–647, 1978.

Twenty-five schizophrenic inpatients receiving antipsychotic medications were evaluated as informed and/or consenting drug consumers by means of a structured interview, and were compared with a matched group of medical inpatients receiving nonpsychotropic drugs. Medical patients were better informed about positive aspects of medication, such as name, dose, and relationship of drug treatment to a specific diagnosis. Schizophrenic patients, however, were significantly better informed about both side effects and risks. Although both groups felt that their medication had helped them, 93 percent of the medical patients but only 56 percent of the schizophrenic patients indicated that they would take the medication if they had the choice. The fact that schizophrenic inpatients readily shared with an interviewer their reluctance to take medication may offer an avenue for detection and intervention to improve prospects for outpatient compliance. (8 references)— Author abstract.

4529. Soskis, D.A., and Jaffe, R.L. (Dept. of Psychiatry, Temple University School of Medicine, Philadelphia, PA 19140) Communicating with patients about antipsychotic drugs. Comprehensive Psychiatry, 20(2): 126–131, 1979.

In a study of communication between physician and patient concerning antipsychotic drugs, male inpatient schizophrenics and their physicians were interviewed about physicians' attitudes toward antipsychotic drugs and patient knowledge, compliance, and therapeutic response. A lack of congruence between what psychiatrists thought they should transmit to their patients and what they actually did was noted. No relationships between physician-patient communication variables and patient compliance were found. (13 references).

4530. Stier, C.S.; Elizur, A.; Yeret, A.; and Davidson, S. (Shalvata Psychiatric Centre, Sackler School of Medicine, Tel Aviv University, Hod-Hasharon, P.O.B. 94, Israel) Anti-autistic and anti-psychotic activity of pimozide in chronic schizophrenic patients undergoing acute exacerbations. Current Therapeutic Research, 23(5):632–641, 1978.

An uncontrolled trial on 14 chronic schizophrenic patients with acute exacerbations, undertaken to evaluate the therapeutic specificity of the drug pimozide in combating the target symptoms of autism, apathy, emotional withdrawal, depression, delusions and hallucinations, is reported. Weekly evaluations were made by two psychiatrists independently during the 10-week study. In 6 out of 12 patients who finished the trial, marked improvement appeared in the second week, and they were able to be discharged from the hospital at the end of the trial period and returned to social and occupational functioning. The main symptoms that showed improvement were thought disorder, apathy, emotional withdrawal, motor retardation, depression, and somatic concern. Four patients failed to respond to the treatment. No ataractic effects were evident, and in two patients, the drug aggravated or even precipitated psychomotor agitation, anxiety, and tension. (17 references)—Author abstract, modified.

4531. Toner, E., and Cabanban, P.A. (St. Francis Hospital, Sussex, England) Schizophrenia: A sense of identity. Nursing Mirror and Midwives Journal, 147(14):35–37, 1978.

Nursing problems of caring for the chronic schizophrenic patient are discussed, and the effects of institutionalization are described as the main problem in the long-term management of schizophrenia. The creation of a large number of chronic, apathetic, institutionalized schizophrenics is attributed to rigid, inflexible, authoritarian methods of ward management. To attain the aim of returning the long-term chronic schizophrenic to some degree of normal life, the patient should be viewed as an active participant—a person limited by damage he has sustained, but striving to achieve satisfaction, security, independence, recognition, and responsivity. (7 references)

4532. Tuma, A.H.; May, P.R.A.; Yale, C.; and Forsythe, A.B. (Clinical Research Branch, National Institute of Mental Health, 5600 Fishers Lane, Rockville, MD 20857) Therapist experience, general clinical ability, and treatment outcome in schizophrenia. Journal of Consulting and Clinical Psychology, 46(5):1120–1126, 1978.

Data systematically collected in the course of a controlled comparison of the effects of five different treatment methods in schizophrenia are presented. Among the 23 outcome variables studied, there was not a single instance in which the effect of therapist experience and general clinical ability was significantly related to outcome. There appeared to be, however, differences among therapists' results that were not related to experience and general clinical ability, particularly in relation to the length of time that they kept their patients in the hospital. It is noted that drug treatment tended to override but perhaps not entirely eliminate these effects. (36 references)—Author abstract.

4533. Turner, S.L. (University of North Carolina, Chapel Hill, NC 27514) Prevailing disability among schizophrenics in community care: Services utilized and social supports reported. Dissertation Abstracts International, 39(1):162–B, 1978.

To measure social supports and evaluate the associations posited between these factors and disabled behaviors, the services utilized and social supports received by schizophrenics in community care in Johnston County, NC, were analyzed. Gruenberg's techniques for ascertaining the presence or absence of severe social breakdown syndromes were used to define disability status of 103 schizophrenics in community care. Significant differences between disabled and nondisabled patients were found on a variety of social support measures. Seventeen percent of the total respondent group stated they would prefer, at least sometimes, to be in a hospital rather than in the community. The pervasive associations found between social supports—home composition, extra household contacts, and an index of qualitative support—and disability suggest the potential usefulness of this index of qualitative social support in clinical or research investigations attempting to evaluate or change socioenvironmental conditions for patients in community settings.—Journal abstract, modified.

4534. Van Putten, T.; May, P.R.A.; and Marder, S.R. (Veterans Administration Hospital, Wilshire and Sawtelle Blvds., Los Angeles, CA 90073) The hospital and optimal chemotherapy in schizophrenia. Hospital & Community Psychiatry, 30(2): 114–117, 1979.

The need for hospitalization of schizophrenics receiving chemotherapy is discussed. It is stated that in some cases chemotherapy of schizophrenics is best monitored in a hospital setting. Dysphoric responders and noncompliers are identified as patients who can most benefit from monitoring in the hospital. Dysphoric responders, whose illnesses have been only minimally responsive to antipsychotic drugs, are in danger of psychotoxicity due to excessive dosage. Habitual noncompliers have little investment in staying well and are unlikely to show even mild drug side effects. The use of the test dose concept to monitor drug response is described. (42 references)— Author abstract, modified.

4535. Watts, G. (New Medical Journals, Ltd., Clareville House, 26–27 Oxendon Street, London SW1Y 4EL England) Molecule à la mode. World Medicine (London), 13(14):35–36, 1978.

The use of β-endorphin by psychiatrists Nathan Kline and Heinz Lehmann to induce changes in schizophrenic and depressed patients is discussed. Experimentation rather than research with 15 patients and one normal subject was an attempt to do something with patients for whom drug therapy had failed. After intravenous injections, the patients' mood and behavior were monitored and

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compared with previously obtained placebo effects. Progressive reduction or disappearance of schizophrenic symptoms and mood change in depressed patients were observed. Distinctions between immediate and delayed influences of the drug are made. Speculation about the mechanism of action of this drug, which is expensive to synthesize, and criticisms of the way the experimentation was conducted are included. A basic question raised by these preliminary findings is how the same substance can produce therapeutic results in patients with different diagnoses.

4536. Wilmer, H.A. (Department of Psychiatry, University of Texas Health Science Center, San Antonio, Texas 78284) A psychologic approach to schizophrenia. Psychiatric Annals, 1(7):15, 19, 23, 27, 31, 35–40, 1977.

A description and evaluation of a psychologic treatment program for schizophrenics is presented. The program has been operating for 4 years in a Veterans Hospital with a therapeutic community composed of adult subacute and chronic schizophrenics. The therapeutic program includes daily community meetings, small group therapy, psychodrama, dream seminars, and family therapy. The most important procedure is the daily community meeting, which was planned to take advantage of techniques learned from previous therapeutic communities with schizophrenic patients. Antipsychotic drugs are not used routinely. The program emphasizes psychologic treatment and interpersonal relations, rather than total reliance on organic treatment. (21 references)

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The *sponsor* should submit a supporting letter setting out in some detail justification for the nomination and summarizing the research accomplishments of the nominee.

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New from Cambridge University Press is **Schizophrenia: The Epigenetic Puzzle, by Irving I. Gottesman and James Shields, with the assistance of Daniel R. Hanson.** The origins of schizophrenia have long baffled those who have to deal with the afflicted. For professionals, the etiology of schizophrenia has been a source of controversy; for relatives and friends of patients, a source of confusion and anguish.

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---

family, twin, and adoption studies and studies of childhood psychopathology; and greatly enhance the usefulness of the book for students. Social biology (marriage, divorce, fertility) and genetic counseling are discussed in easily understandable terms.

The authors' cogent presentation and stimulating conclusions about future directions for research on schizophrenia will be of interest to a wide range of clinical researchers and their students.

Irving I. Gottesman is Professor of Psychiatric Genetics at the Washington University School of Medicine in St. Louis. The late James Shields was Reader in Psychiatric Genetics at the Institute of Psychiatry, London.

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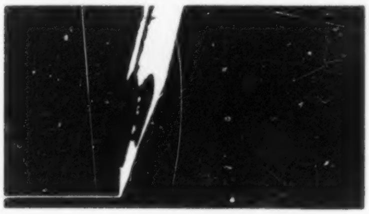

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Schizophrenia Bulletin National Institute of Mental Health

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About the Cover

The *Schizophrenia Bulletin* features art done by current and former mental hospital patients. The painting that appears on the cover of this issue was sent to us by Yvonne Markowitz, Ed.M., ATR, Worcester State Hospital, Worcester, Massachusetts. The artist, Damian H. Judd, has provided the following description of his drawing:

I had been a patient on the Fitchburg-Leominster Unit of Worcester State Hospital for approximately 3 months when I produced this charcoal and pastel drawing in art therapy. It represents the difficulty I experienced in expressing feelings during my hospitalization.

VOL. 8, NO. 4, 1982

Thought Disorder or Speech Disorder in Schizophrenia?

by Elaine Chaika

At Issue

Abstract

The classification of schizophrenic patients into thought disordered (TD) and non-thought disordered (NTD) is questioned. It is suggested that the terms speech disordered and non-speech disordered are more exact, and that viewing deviant speech structurally with no assumptions as to the thought behind it may prove valuable.

Some psychiatrists characterize the population of schizophrenics as being either thought disordered (TD) or non-thought disordered (NTD). Rochester and Martin (1979, pp. 4–6, 169) argue convincingly that the diagnosis of TD is circular since it depends upon the patient's speech. In their words, "The clinician proceeds from a personal experience of confusion to infer that the patient is confused" (p. 169). However, many argue, as does Holzman (1978, p. 373), "Speech is, after all, spoken thought." Hence, in this view, confused speech is an indication of confused thought.

There are several problems with an automatic equation of speech with thought, however. First, speech and thought are not always identical. One may think one thing and say quite another, or say nothing at all.

Second, not all speech conveys thought. For instance, greetings, rituals, and idle chitchat—what Malinowski (1923) termed *phatic communication*—often convey no thought. Such speech is employed for social bonding, to fill up the awful silences.

Third, language is partly a self-contained system with no inherent reference to thought or the outside world. That is, language has an independent structure of its own—actually, four interrelated structures: phonology, syntax, semantics, and discourse. The sound system of language is wholly self-contained. The sounds used in a given language and the rules for allowable combinations of sounds into syllables are arbitrary, having no necessary relation to the physical or cultural world. Even supposedly onomatopoeic sounds vary considerably from language to language, proof that they, too, are arbitrary conventions, not actual reproductions of sounds in the environment. Many rules of syntax are also self-contained. For instance, whether a language habitually places direct objects before or after verbs, whether it uses prefixes, suffixes, or word order to indicate the function of a word in a sentence, or the particular manner in which a language forms questions is arbitrary, explicable only in terms of the language system itself. Both sounds and syntactic rules are in themselves meaningless. It is the special genius of human language that meaningless elements and rules can produce meaningful structures. This means that errors in speech production may proceed from errors in rule application with no necessary implication for other thought processes.

It is not until we are at the level of semantics that language interfaces with the world or the individual's intent and desires, or both. It is true that phonological and syntactic rules, by forming words and sentences, contribute to semantics, but the rules themselves are self-contained and arbi-

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trary. This means that speech can go awry at these levels, as it does in aphasias and dementias, without other intellectual functions necessarily becoming impaired. That is, damage may occur to the part(s) of the brain which is responsible for the storage and application of such rules, but leave other parts intact. Or, all may be impaired. The point is that disordered speech does not necessarily indicate disordered thought as well. It only may, in some instances.

Fourth, thoughts cannot be directly observed, although speech can. If speech shows structural deviance, that does not constitute proof that thought does. It is possible for normals to create nonsense words and sentences although their thinking processes may be intact. The classic example is Lewis Carroll's *Jabberwocky,* which is structurally normal, but has words that do not happen to appear in the language. So far as we know, the ability to produce this kind of nonsense is part of one's natural linguistic ability. Conversely, one can create structurally abnormal sentences from known words, such as "Am girl yesterday went come boy," or one can produce total gibberish, as Sid Caesar and Danny Kaye did in their comedy routines. None of these deviant productions necessarily indicate any dysfunction in thought. The opposite may also be true. A patient might utter structurally normal sentences which indicate impaired cognition. For instance, one patient whom I observed used normal language to inform his psychiatrist that chipmunks brought him his secret language in seeds. Another complained, "That tape recorder is reaching out and destroying my brain cells." Such utterances indicate either hallucinations, grossly impaired ability to deduce cause and effect, or failure to discriminate between animate and inanimate objects—all apparently failures in thought. Conversely, structurally deviant speech might contain perfectly logical thoughts that are appropriate for the matter at hand. For instance, one patient, a salesperson, responded to my question, "Do you give discounts?" with "Yes, I'm 75 percent, 50 percent." He also told me he thought that I could help him because "You're an open system. I'm an open system." As deviant as these utterances were, they did make sense. The patient evinced a general confusion between related words (Chaika 1974, 1976). The first utterance meant "I give 75 percent, 50 percent [discount]," and the second seemed to mean that both he and I were open people; we, therefore, had open systems. Perhaps a more dramatic instance of structural deviance not necessarily correlating with illogic is the following production in response to the question of where the patient lived and what he did there:

> Mill Avenue is a a house in between Mill Avenue is a house in between Avenues U and Avenue T I live on Mill Avenue for a period of for now a period of maybe fifteen years for around approximately fifteen years I like the fam- I like every family on Mill Avenue in the world I like every family in the United State of America I like every family on on Mill Avenue I like Mill Avenue is a is a block with that is busy cars always pass by all the time I always look out the window of my front porch front porch at time when I s- when I'm not sure if it's possible about the way I think I could read their mind about people's society attitude plot and spirit.[1]

The patient not only names his place of residence but gives its exact location. Since he does, indeed, live in New York City, it is entirely possible that this is on a block which has cars passing by all the time. He also states that he likes his neighbors and everyone else in the world, and that when he looks out the window, he is not sure if he can read people's minds about their attitudes, plots, and spirits. One might argue about the paranoia in such a statement, and assuredly one can analyze the structural deviance. However, everything he says seems to be true, or is potentially true. This is not to say that such patients are not thought disordered. It is only that structurally deviant speech alone is not sufficient grounds to categorize thought disorder. If the semantic content of the speech can be deduced, and if it is illogical, or if the patient performs poorly on cognitive tasks, then one can assume that thought is not functioning properly. Otherwise, structurally deviant speech should be taken as evidence of temporary or permanent impairment in linguistic production itself. Until and unless experimentation confirms that thought and speech are identical—and thus far this has not been proven—one cannot assume that a break in one automatically indicates a break in the other (e.g., Oleron 1953; Lenneberg 1953; Furth 1961; Johnson-Laird and Wason 1977). Indeed, one's thoughts must be separate from one's speech, preceding it, for how else could one choose the exact words and syntax one wished to convey one's meaning?

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[1] Courtesy of Dr. Bonnie Spring, who does not necessarily concur with any views expressed in this article.

Fifth, the very concept "thought" is ill-defined. What is a thought? Is it equivalent to a word, a phrase, or a sentence? Since many sentences are actually composed of two or more smaller sentences, is there a thought for each of the sentences contained in one, or is there only one thought for the entire sentence? For instance, the sentence "I know Max is a slob" is composed of two deep structure sentences, "I know something" and "Max is a slob." How many thoughts are conveyed? One? Two? Eight? If one claims that thought and speech are identical, and that disruption in speech always indicates disruption in thought, then one must be able to correlate the concept of thought with speech structures.

Sixth, every language has ambiguous statements and paraphrases (equivalent statements). In themselves, these show that thought and language are not identical. If one statement, such as "exciting women can be dangerous" can convey at least two separate thoughts, and if one thought can be stated in more than one way, then thought and speech cannot be identical.

Moreover, normals frequently make slips of the tongue and other errors in speech production. If speech and thought were one and the same, these would always indicate disruptions in thought processes, a conclusion few would care to make. Rather, it is usually assumed that such errors proceed from momentary lapses in retrieving correct words or sounds, or lapses in self-monitoring (Fromkin 1971), and that such errors cast light on the nature of language storage in the brain.

It should be noted that those patients who do produce abnormal speech during psychotic bouts may themselves verify that such speech does not reflect their actual thoughts. Chapman (1966, p. 236) presents several such comments. A patient I observed commented after seeing himself on videotape that it was no wonder that people couldn't understand him. He claimed that he never realized that his speech was so strange. Rather, when he had heard tape recordings of his speech, he had assumed that the recordings were distorted.

Seventh, to call some schizophrenics TD on the basis of structural abnormalities in their speech is to imply that those who do not evince such abnormality have no thought disorder. It also implies that any person who evinces structural abnormality in speech is thought disordered. However, aphasics with known lesions are not usually termed TD despite the fact that their speech often is as disordered as that of TD schizophrenics. It is often difficult to distinguish between the speech of the two populations (Benson 1973; Chapman 1966; Chaika 1977, 1982). This does not mean that aphasics may not show other cognitive impairment (e.g., Lesser 1978, p. 57), but even when they do, it is not always clear that it is the disruptions in the language faculties alone that cause the deficit. Damage to surrounding tissue may also be implicated. The point is not that cognitive impairment does not occur in aphasics, it is that no necessary assumption is ever made that it has. This does not mean that language is completely divorced from thought and cognition. Certain intellectual abilities, such as breaking stimuli down into component parts and resynthesizing them, do seem to be tied to language. Still, as yet, we do not fully understand the complex interplay between language and thinking. The study of cognitive defects in aphasias is increasing our understanding, but, so far, not enough so that we can extrapolate from intermittent error to thought. Until we can, basing judgments of thought disorder on the basis of dysfunction in structure of speech is not only circular and unwarranted but obscures some very real issues, as shown below.

Those schizophrenics who do evidence structural abnormality in their speech show several kinds of disruption: neologizing, gibberish, word salad, inappropriate rhyming, alliterating, and associating, as well as repetitions of words or phrases. Admittedly, some of these are rarer than others, but all have been reported frequently in patients diagnosed as TD schizophrenics. I have elsewhere shown that all of these constitute structural abnormality in speech production (Chaika 1977, in press). The questions to be answered, then, should be "In what ways are these abnormalities related?" and "Why are some more common than others?" One might also inquire why some diagnosed schizophrenics do not evince peculiarities in speech, and also what relation speech dysfunction may have to the hallucinations also common in this illness. Then, too, one might ask why schizophrenic speech dysfunction is sometimes similar to that of patients diagnosed as manic (Andreasen and Powers 1974; Chaika 1977). It is not to be supposed that the answers to these questions will necessarily lead to a complete explanation of all schizophrenic behaviors. However, they will at least take one confusing set of data, the disparate speech deviations of some schizophrenics, and account for them. Then, perhaps, the explanation for the speech disruption can be correlated with other schizophrenic behaviors.

It must be emphasized that experimental procedures such as word association tests (e.g., Bannister 1960; Chapman, Chapman, and Daut 1976) cannot yield the answers to these questions as normal speech is not produced by associating one word with another. However important it is that schizophrenics are more likely to give dominant responses or that they do not have fixed constructs, these do not explain errors in word formation, especially gibberish and neologisms, inappropriate rhyming and alliterating, or word salads, much less the intrusion of extraneous matters into a discourse (what is often termed derailment). Speech has to be analyzed in terms of what we know about normal speech production and comprehension. Either freely produced speech or speech produced under experimental conditions that elicit actual discourse is appropriate for such analyses (e.g., the procedures of, but not necessarily the explanations by, Singer and Wynne 1965; Rochester and Martin 1979; Cohen 1978).

An ordinary application of Occam's razor demands that the simplest explanation for the diverse peculiarities of schizophrenic speech behaviors must be the one adopted. Since all are observable speech production errors, it seems to me most profitable to consider them as evidence of speech disorder, not necessarily thought disorder. It also seems to me that they should be examined in the light of what we do know about normal speech production, as well as normal error. This position is reinforced by the fact that when we are able to decode schizophrenic speech, often despite our feeling that it is structurally deviant, the thoughts expressed are quite ordinary (Chaika 1974, 1977). And, as illustrated above, bizarre ideation can be expressed in structurally normal speech.

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Two back issues of the *Schizophrenia Bulletin* are available to requesters:

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Letters to the Editor

To the Editor:

In response to your invitation to comment on the recent article by Dr. Roger Blashfield "Feighner et al., Invisible Colleges, and the Matthew Effect" (*Schizophrenia Bulletin*, 8:1–6, 1982), I have the following comments.

An additional sociological contribution to the high rate of citation of the important article by Feighner et al. should also be considered. As a reviewer and editor of journals in which manuscripts have cited this article on diagnosis, I have often wondered whether the citation always assured one that careful and critical diagnostic appraisals had, in fact, taken place. Is it possible that the citation of an increasingly acceptable standard reference in a prestigious journal has had elements of incantation of a code word, aimed at increasing the probability of favorable editorial review and reader acceptance? Evidence to support this occurrence includes the observation that categories were sometimes included in manuscripts (and even in some published articles) that *did not exist* in the St. Louis diagnostic system (e.g., "acute schizophrenia")! In addition to citation of a standard diagnostic reference, it would help editors and readers if authors of clinical reports would, more routinely, actually describe the salient characteristics of patients they have studied. This approach would be particularly helpful to foreign or future readers who may not be familiar with diagnostic criteria currently in vogue in this country.

It was an interesting and provocative article and series of responses to it for which you are to be complimented, refusals of the article by several other journals notwithstanding.

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To the Editor:

According to Roger K. Blashfield, (*Schizophrenia Bulletin*, 8:1–6, 1982), a small group of researchers, part of an invisible college, have advocated a "neo-Kraepelinian approach to classification" and their influence on American psychiatry has been profound. I am cited in this article as a "prominent member" of this college. The article also lists the neo-Kraepelinian credo, nine articles of faith, according to my good friend Gerald Klerman. I take this opportunity, in the hallowed pages of this distinguished journal, to offer my resignation publicly from the neo-Kraepelinian college as I do not subscribe to two of these articles of faith.

Article five states: "There are discrete mental illnesses." As stated in one of the required texts of this college, *DSM-III*, "In *DSM-III* there is no assumption that each mental disorder is a discrete entity with sharp boundaries (discontinuity) between it and other mental disorders, as well as between it and No Mental Disorder." This is an empirical issue and the available evidence supporting discontinuity among the functional disorders, such as Affective Disorders and Schizophrenia, is far less than compelling.

Article six states: "The focus of psychiatric physicians should be particularly on the biological aspects of mental illness." Nonsense. Psychiatrists should concern themselves with all aspects of mental illness, including the psychological and social aspects.

I hope that my resignation from the neo-Kraepelinian college will be accepted, as I have already joined the faculty of a much larger institution of higher learning. The faculty of this university is multidisciplinary and its credo is simple and easy to remember: it is "data-oriented," a term suggested by another good friend of mine, Arthur K. Shapiro. Faculty and students of this university are harmoniously committed to the pursuit of data that will help us understand the multiple determinants of mental illness and the relative effectiveness of various biological, psychological, and social treatments.

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To the Editor:

Blashfield (*Schizophrenia Bulletin*, 8:1–6, 1982) developed the case that social factors contributed to the importance of the article by Feighner et al. (1972) on diagnostic criteria. He measured the importance by numbers of citations. The factors included: (1) acceptance by a prestigious journal, the *Archives of General Psychiatry;* (2) the Matthew effect: to those who have shall be added unto—when you are widely quoted you will be more widely quoted; and (3) the invisible college effect: the initial fans were closely related professional workers from prestigious departments devoted to the biological outlook.

In a way, Blashfield adds another factor, acceptance of the neo-Kraepelinian's credo. This he effectively quotes from Klerman's (1978) nine tenets: we are not all patients, there are discrete mental illnesses, statistical techniques should be favored, etc., etc. Nevertheless, and despite all this, Blashfield still perhaps pussyfoots and almost misses the jugular. He writes that he did not imply that "scientific merit was unrelated to the wide impact of the Feighner et al. article. Historians of science generally agree that the alterations in a science rarely result from either cognitive or noncognitive factors alone (MacLeod 1977)."

We feel anxious to emphasize that even the attempt to separate cognitive and noncognitive factors is to answer covertly some of the most central intellectual issues involved. Therefore, while writing to support Blashfield, we want to go further.

We would, for example, want to suggest that Kendell's (*Schizophrenia Bulletin*, 8:11–12, 1982) discussion of Blashfield is optimistically unpsychiatric in hoping that "intellectual considerations are probably more important than personal rivalries in favoring those who subscribe to the dominant paradigm."

Perhaps Katz's (*Schizophrenia Bulletin*, 8:9–11, 1982) comments come nearer to what we want to say. He emphasizes three needs for different psychiatric nosologies: the physician to treat, the psychopathologist to discuss etiology, and the scientist to discuss the natural order. He surprisingly omits the needs of the patient, the patient's relatives, the police, and the patient's neighbors, and, presumably because he hadn't read it, he doesn't discuss the operational need for categories, which Kendell implies, nor therefore what Kendell means by Feighner's major technical advance. For Aristotle a technology is a means to a defined end; it is to be contrasted with science or surveying horizons. The end involved here seems to us to be a categorization and medicalization of men. The classification is necessary if you want that sort of knowledge; otherwise *a* classification is not needed, nor is *an* operational definition.

Katz, seeing this point, still doesn't go on to state that physicians can have the classification they want for the treatment they like, psychopathologists for their chosen etiologies, and pure scientists have the greatest menu of all from which to choose their meal when they feign to be involved in pure thought. The latter is something to which Katz also seems to aspire in his recommendation that: "It may be time to rise above the social issues, to reexamine the problem in a more scholarly context, possibly a new NIMH sponsored conference on 'the state of research on classification in psychopathology.' " Our optimistic hope to be invited to yet another conference is felt, despite our conviction that the money could be better, though less pleasantly, spent for us, or the others (more) fortunate to be invited.

It seems so hard for the medical person to believe and accept different possible sciences and to see our choices of one or the other as affected by our vision of life and its/our purposes. Yet we feel one of the few things one can almost prove is the impossibility of a truly objective nosology. That is a contradiction in terms precisely because classifications are for purposes. That is not to espouse total relativism but to see our thoughts as dialectical; creating while describing. Bachelard (1966) speaks of the polemic of reason against reality and Nelson Goodman (1978) develops it in *Ways of Worldmaking*.

Unfortunately, busy clinicians are hard put to pause long enough to be less naive, if we may be so arrogant as to say so. In amelioration, we do confess much of the searchlight must be on us, our conferences, books, publications, thoughts, selves, and our need to be the ones in print.

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To the Editor:

The behaviors Dr. Thomas H. McGlashan ("Aphanisis: The Syndrome of Pseudo-Depression in Chronic Schizophrenia," *Schizophrenia Bulletin,* 8:118–134, 1982) elaborately describes as evidence of aphanisis seem to me to be subsumable under the traditional headings of blunted affect or emotional blunting as reviewed by Abrams and Taylor (1978) and Andreasen (1979). These articles include clear definitions and reliability data regarding the affective disturbance in schizophrenia. I believe the distinction, if any, between aphanisis and these traditional terms requires clarification, before a new descriptive label is introduced.

When Dr. McGlashan prepared his original 1979 presentation, the aforementioned papers were probably unavailable, but they deserved mention in the 1982 *Schizophrenia Bulletin* publication.

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Erratum

The article by John L. Haracz entitled "The Dopamine Hypothesis: An Overview of Studies With Schizophrenic Patients" (*Schizophrenia Bulletin,* 8:438–469, 1982) contains a misplaced section of text that should be deleted. The misplaced text begins on p. 452 with the paragraph "The failure to find a universal biochemical . . ." and extends to p. 453 including the paragraph which begins with "A nondopaminergic etiology. . . ." Furthermore, a sentence on p. 456 should be deleted. This sentence begins at the bottom of the second column and reads as follows: "Schizophrenics with a positive family history of schizophrenia did not differ in platelet MAO activity from schizophrenics with no such family history (Belmaker et al. 1978)."

What Is Schizophrenia?

Editors:
John S. Strauss,
Malcolm B. Bowers, Jr.,
and Samuel J. Keith

Contributors:
Solomon H. Snyder
Seymour S. Kety
Michael J. Goldstein

One of the main questions related to schizophrenia is, naturally enough, what is it? Such a question may seem obvious, naive, impossible, or any combination of these. And certainly it is a bit demanding to expect that anyone could say what schizophrenia is in 1,000 words. On the other hand, we felt that it was worth the effort. We hope that presenting these brief discussions on "what is schizophrenia" by persons who have worked extensively in the field will allow the reader to note areas of overlap and disagreement as well as variations in emphasis. Although no one may yet be able to provide the definitive answer, at least this collection of informed opinions may help clarify the major questions. The group of essays by Solomon H. Snyder, Seymour S. Kety, and Michael J. Goldstein is the second in this series. Further collections of these statements will be presented in subsequent issues. Readers' responses and comments are cordially invited.—*J.S.S., M.B.B., and S.J.K.*

As a psychopharmacologist, I suppose my perspective on schizophrenia should be from the point of view of drugs. In fact, my first interest and involvement in schizophrenia research began when, as a freshman in medical school, I worked under the supervision of David Rosenthal at the National Institute of Mental Health conducting perceptual-motor studies of schizophrenics and reviewing the literature on psychological abnormalities (Snyder 1960; Snyder, Rosenthal, and Taylor 1961). What impressed me was how differently schizophrenics seemed to perceive the world as compared to normals, even in such a seemingly neutral task as Gestalt tests of perceptual closure, filling in gaps in perceived houses and stickmen. At a human level, I was struck by the suffering which had by no means been abolished despite the considerable number of neuroleptics to which the patients were exposed even then in 1959.

All of these impressions have remained with me now some 22 years later. Through the course of medical, psychiatric, and research training, I have not ceased to wonder at what extraordinarily unique alteration in the brain can account for human beings having their mental life sometimes consumed with visual or auditory hallucinations, delusions, and a fundamentally peculiar way of perceiving and thinking about the world.

What has biochemical research into drug action in schizophrenia taught us about the nature of the disorder? Of all the neurotransmitter systems explored in schizophrenia, the most compelling evidence for relevance to the disorder has to do with studies of dopamine. It is reasonably well accepted that a major antipsychotic action of the neuroleptics involves blockage of dopamine receptors. The relative potencies of neuroleptics in blocking one subtype of dopamine receptors, the D-2 receptors, correlate closely with clinical potencies of the drugs and their potencies in animal pharmacological tests which predict clinical antipsychotic effects (Creese Burt, and Snyder 1976; Seeman et al. 1976). These effects are by no means fortuitous, since the very considerable potencies of neuroleptics in blocking receptors for other neurotransmitters such as histamine, α-adrenergic, and serotonin receptors do not show any significant correlation with antipsychotic effects (Peroutka and Snyder 1980).

The other aspect of the dopamine story has to do with effects of stimulants. Amphetamine and related agents in large doses produce a psychosis which can be clinically indistinguishable from acute paranoid schizophrenia (Angrist and Sudilovsky 1978). The problem with amphetamine psychosis as a model of schizophrenia is that it mimics only one subtype of the disorder, and some investigators feel that it is not a perfect model. Thus, some researchers feel that patients with amphetamine psychosis do not display the classic schizophrenic abnormality in affect or thinking. On the other hand, the fact that amphetamine psychotics can fool very experienced psychiatrists into a diagnosis of schizophrenia in the absence of drug history argues in favor of some relationship. Perhaps more impressive than amphetamine psychosis is the finding that small doses of amphetamines can floridly exacerbate specifically schizophrenic symptoms without affecting in a marked way symptoms of patients with manic-depressive illness or neurosis (Janowsky and Davis 1976).

Amphetamines exert their actions by releasing catecholamines or blocking their reuptake inactivation. Some indirect evidence suggests that the amphetamine effects upon schizophrenic symptoms involve dopamine more than norepinephrine. Thus, methylphenidate is more effective than amphetamine itself in worsening schizophrenic symptoms and acts more upon dopamine than norepinephrine.

If blocking actions of dopamine alleviates schizophrenic symptoms while enhancing dopamine effects worsens them, we have a "dopamine hypothesis" of drug actions in schizophrenia. It should be emphasized that this by no means establishes that dopamine systems are specifically abnormal in schizophrenia. The fundamental abnormality might be in some other system which is somehow linked to dopamine neurons. Only a direct demonstration of abnormalities in schizophrenic brain could answer this question. Measurements of dopamine itself have shown some possible abnormalities, but results are inconclusive (Bird, Spokes, and Iversen 1979). If schizophrenics are hypersensitive to dopamine, perhaps they have too many dopamine receptors. There have been reports of increased numbers of dopamine receptors in schizophrenia (Lee et al. 1978; Owen et al. 1978), but in recent studies controlling for drug dosage we have obtained evidence that these effects are in fact secondary to the well-known capacity of chronic neuroleptic administration to augment numbers of dopamine receptors (Burt, Creese, and Snyder 1977; Mackay et al. 1980).

Of course, those who would search for a specific biochemical abnormality in schizophrenia must bear in mind the considerable likelihood that schizophrenia is heterogeneous. If there are 10 or more distinct diseases which all share the symptoms of schizophrenia, then the likelihood of finding the specific abnormality in any one of these forms is lessened considerably. Nonetheless, it is possible that patients with classical clinical symptoms of schizophrenia and a strong family history all suffer from a single disease entity. At a minimum biochemical investigations should pay close attention to clinical distinctions of subgroups based on symptoms, family history, course, or age of onset (Bird, Spokes, and Iversen 1979).

In any event, though we cannot assert any causal relationships, dopamine does seem to play a role in mediating drug actions in schizophrenia and is somehow linked to systems that are abnormal in schizophrenia. I continue to be impressed with the fact that the relief of schizophrenic symptoms by neuroleptics is rarely total. How might we go about finding out the fundamental abnormality? Sifting through schizophrenic urine, blood, and spinal fluid is probably more difficult than looking for a needle in a haystack. Understanding how drugs act in schizophrenia has been more heuristic. Accordingly, since neuroleptics are far from a panacea, I would advocate major efforts toward developing antischizophrenic drugs acting by novel mechanisms. This represents a challenge to the drug industry, since presently used animal tests merely select for dopamine receptor blocking activity. Nonetheless, a variety of biochemical and pharmacological strategies can be employed. Once new and effective drugs are available, we would hope to find out how they act, an endeavor which in turn might provide clues to what is fundamentally wrong in the schizophrenic brain.

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Progress in all of the branches of medicine has depended upon accurate and perceptive observations with the tools at hand and an intellectual process similar to that which developed in other branches of science for the recognition of common features or unifying concepts and the formulation and evaluation of hypotheses. Before gross, microscopic, or chemical pathology was able to differentiate morbid processes, and microbiology, biological chemistry, toxicology, or epidemiology had advanced sufficiently far to identify etiology and pathogenesis, a groundwork had been laid by phenomenological syndromes defined simply on the basis of common course and symptoms and the presumption which this suggested of common features in the underlying pathology, if not etiology. Many of the descriptions of these syndromes are among the classics in medicine and made further progress possible as new methods of observation were developed.

In psychiatry, the syndrome of schizophrenia is the most venerable and one of the most useful of these phenomenological clusters. It had its inception in the closing years of the last century when Emil Kraepelin observed that syndromes previously described as hebephrenia, paranoia, and catatonia had enough important features in common to permit their conceptualization as parts of a single and broader syndrome which he called dementia praecox. Recognizing that "... there is in the domain of psychic disorders no single morbid symptom which is thoroughly characteristic of a definite malady," he emphasized that "... the composition of the *entire picture* made up of its various individual features, and especially also the changes which it undergoes in the course of the disease..." was necessary for its differential diagnosis and ultimate understanding (Kraepelin 1913, p. 257). In conscientious detail he described the major features and more than 50 individual symptoms which together characterized the syndrome.

Eugen Bleuler (1911), a contemporary of Kraepelin who maintained cordial relations with him, was quick to recognize the importance of Kraepelin's contribution, elaborating upon it and giving it a new name—schizophrenia. He was careful to point out that the whole idea originated with Kraepelin and that almost exclusively to his work was to be attributed the grouping and description of the separate symptoms. He could not, however, "... shirk the uncomfortable duty of coining a new name for this disease ... the present one seems to be awkward." In their separate textbooks and monographs, they described the "fundamental" and "accessory" features, that is, the characteristic and the nonspecific manifestations which several generations of psychiatrists throughout the world found useful in recognizing the syndrome and differentiating it from others, particularly manic-depressive illness. The differentiations, it is true, were imperfect, but not notably more so than those among many medical syndromes when they had to depend only on clinical observation. Neither of the originators thought they were describing a single disease but a syndrome of heterogeneous etiology (Bleuler called it "the group of schizophrenias") with common "morbid processes" which probably accounted for the symptomatic features they had in common.

It would be well to review the "schizophrenic symptoms" which Kraepelin and Bleuler described because of a recent tendency to reject them. The syndrome was described as "a specific type of alteration of thinking, feeling and relation to the external world which appears nowhere else in this particular fashion." Among the characteristic symptoms were "weakening of judgment, of mental activity and of creative ability, the dulling of emotional interest and the loss of energy ... loosening of the inner unity of intellect, emotion and volition in themselves and among one another..." In their further characterization they described disorders of association, incoherence or blocking of thought and speech, impoverishment of affect, inappropriate affect, inability to establish affective relationships with others, a tendency to divorce oneself from reality, bizarre and tangential thinking, stereotypies, and mannerisms and tics of various sorts. An insidious onset in adolescents and young adults with various premorbid difficulties was noted in a large majority of cases, as was a prolonged course and dementia, or at least a failure to return to earlier levels of intellectual integration. Particular types of auditory hallucinations and delusions were described and their frequency pointed out, although both Bleuler (p. 204) and Kraepelin (p. 248) emphasized that hallucinations and delusions were present in many psychoses and were not of special importance in diagnosing the presence of schizophrenia. Recent studies (Carpenter, Strauss, and Bartko 1973; Pfohl and Winokur, in press) which took into account manifestations of schizophrenia as described by Kraepelin and Bleuler found them to be consistent and effective in differentiating that syndrome from manic-depressive illness and other types of psychosis.

Over the past 50 years two trends have developed around or within the original concept of schizophrenia. On the one hand, syndromes were found which resembled the classical syndrome only in certain characteristics, and these were appropriately designated by terms which expressed both their similarity to and separation from the classical syndrome. These have included "schizophreniform psychosis," "schizoaffective disorder," and "schizoid personality." Sometimes terms were adopted which assumed a relationship to schizophrenia which was not conclusively established, such as "latent," "borderline," "atypical," "pseudo neurotic," "acute," or "good prognosis" schizophrenia. A serious epistemological infraction, however, came from Schneider (1959) who completely altered the concept of schizophrenia but retained its original name. Features regarded by both Kraepelin and Bleuler as fundamental and specific (impoverishment of affect, disturbances in personal contact and rapport, ambivalence, lack of volition, depersonalization, and stereotypies) he specifically rejected and arbitrarily established one of the first "operational" diagnoses of schizophrenia, restricted to particular types of hallucinations and delusions which Bleuler and Kraepelin had regarded as accessory and nonspecific. No attempt was made originally to demonstrate that Schneider's "first rank symptoms" successfully and more economically described the original syndrome, and where that crucial assumption has been tested more recently in several studies, the first rank symptoms have not been shown to be either characteristic or discriminating. The resultant disillusionment has led some to disparage the value of "schizophrenic symptoms" in diagnosis, but the evidence which has been adduced to defend that position has rested almost entirely on Schneider's criteria rather than the detailed descriptions of Kraepelin and Bleuler, who alone had the right and the responsibility to define the syndrome they had delineated or named.

Because of the accretions to the original syndrome, parochial differences in emphasis or interpretation of the symptoms as originally described, and a willingness on the part of some to accept entirely different criteria for diagnosis, there has emerged a need to establish some minimal standardized description of the syndrome and putative subtypes. In doing so, it has been relatively easy to measure reliability or agreement between raters, and by specifying very concrete and obvious symptoms to enhance that reliability. Establishing the validity of these more parsimonious descriptions, however, is much more difficult. The most appropriate procedure in the case of a syndrome established entirely by clinical phenomenology would be to test the reliability of diagnoses made by the suggested criteria against diagnoses which would have been made by Kraepelin and Bleuler or, in the absence of that ultimate validation, by careful attention to tenets they established in their writings. That has rarely been done and the usual practice is to make use of a consensus of psychiatric opinion. Since that varies over time and from one school of psychiatry to another, the standardized operational concepts of schizophrenia have also varied, sometimes in contradiction of emphatic caveats by the original founders of the syndrome. Bleuler anticipated that problem 70 years ago: "Naturally nothing is gained thereby except another symptomatological picture which is then called a disease and which moreover is misleadingly defined by the same terms as the qualitatively and quantitatively quite different Kraepelinian concept" (p. 278). Strauss and Gift (1977) recently applied a number of operational definitions of schizophrenia to the same group of 272 patients with sobering results. The number of those patients selected as "schizophrenic" varied from 4 to 68! The value of standardized operational diagnostic strategies lies mainly in the economy that they offer in description and communication. The description of the syndrome which each provides is necessarily arbitrary and incomplete and offers little reason for assuming that any one of them defines "true" schizophrenia.

The *DSM-II* (American Psychiatric Association 1968) definition of schizophrenia encompassed the descriptions of Kraepelin and Bleuler but deviated in including "acute schizophrenia," which is characterized mainly by hallucinations and delusions, despite Bleuler's admonition that these are "partial phenomena of the most varied diseases whose presence is often helpful in making the diagnosis of a psychosis, but not in diagnosing the presence of schizophrenia." Our study of schizophrenic adoptees and their biological and adoptive relatives used global diagnoses based on *DSM-II* and Bleuler's descriptions. Although milder but chronic schizophrenia-like disorders (latent and uncertain schizophrenia) were found to be concentrated in the biological relatives of chronic schizophrenic adoptees, this was not the case for acute schizophrenia. These results would have been anticipated by Bleuler (Kety 1980).

DSM-III (American Psychiatric Association 1980) recognizes the fundamental schizophrenic symptoms of Kraepelin and Bleuler and attaches considerable importance to them in its narrative description of the characteristic features of schizophrenia, while giving them less weight in the minimal required criteria than a number of accessory symptoms. By removing "acute schizophrenia" and recognizing a chronic course and deterioration from a previous level of functioning, it has come closer than *DSM-II* to Kraepelin's original concept, but has also removed "simple schizophrenia," which both Kraepelin and Bleuler had recognized as a form of schizophrenia, including it with "latent schizophrenia" under the rubric of "schizotypal personality disorder."

The *DSM-III* criteria and the earlier Research Diagnostic Criteria have recently been subjected to the crucial test of validity by applying them to patients described and diagnosed by Kraepelin (James and May 1981) and have stood up reasonably well, especially in the case of the more typical chronic schizophrenics or manic-depressives. Where characteristic features of both illnesses are present, *DSM-III* would make a diagnosis of schizophrenia if the schizophrenic manifestations preceded those of affective disorder or were of longer duration. Bleuler would have gone even further in rejecting the significance of affective symptoms: "All of the phenomena of manic-depressive psychosis may also appear in our disease; the only decisive factor is the presence or absence of schizophrenic symptoms" (Bleuler, p. 304).

If, as appears likely, both schizophrenia and major affective disorder are syndromes of heterogeneous etiology and pathology, the occurrence of some cases which have characteristics of both is not surprising, and assigning them to one or the other syndrome on the basis of clinical symptoms alone will necessarily be arbitrary. The existence of pure forms of the two syndromes, however, suggests that there are different malfunctioning systems or processes in the brain which are involved in each, resulting from different or even the same etiological factors. In the case of numerous medical and neurological disorders, a particular etiological process may affect different organs, systems, or processes resulting in different symptomatic syndromes, pure or mixed, depending on the degree and complexity of involvement. Where we add to this the recognition that different etiological factors may affect the same system producing a similar symptomatic picture, the distance between describing the syndromes and elucidating the underlying etiologies and pathologies becomes apparent. The numerous and often arbitrary redefinitions of the clinical picture of schizophrenia which have taken place in the past 75 years have not reduced that distance appreciably. There is reason to hope, however, that new information obtainable by recently developed approaches in genetics, immunology, morphology, biochemistry, physiology, pharmacology, and psychology, insofar as they are able to associate clinical features with underlying processes, may bring us closer to that goal. In fact, some progress based on each of these disciplines is now apparent.

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I find it easiest to conceptualize schizophrenia from a life span developmental perspective. A person who develops a schizophrenic reaction in late adolescent or early adult years typically faces a major developmental task involving a transition from one life role to another. Thus, psychotic breaks most frequently occur in the last year of high school or shortly after graduation, during the freshman year of college, or shortly before or immediately after college graduation. For those who do not pursue higher education, similar transition points such as entry into the job market or armed services are correlated with a psychotic breakdown.

The search for specific, acute life events which trigger the psychotic break has not always been successful as the developmental transition points associated with a schizophrenic reaction are frequently normative stressors for all young people rather than extraordinary in nature. When extraordinary life events precede a psychotic break, these have important prognostic implications.

Since most schizophrenic reactions are associated with demands for separation from one's nuclear family, independent vocational functioning, or heterosexual acceptance and adequacy, how can we account for the preschizophrenic individual's particular vulnerability to these life demands? The vulnerability model of Zubin and Spring (1977) provides me with the best scheme for answering this question. My own clinical and research experience suggests that persons at risk for subsequent schizophrenia vary widely in their biological risk for the disorder based upon evidence from family history data or obvious trauma to the brain at birth. Consider a case with notable biological vulnerability: Jimmy was born after 50 hours of difficult labor with obvious signs of anoxia present and a poor Apgar score. From his earliest years he was diagnosed as brain damaged, with particular deficits noted in perceptual-motor integration and short-term memory. As his father described him, Jimmy was well coordinated and could hit a baseball solidly, but he couldn't remember how to run around the bases once he hit the ball. Jimmy went to excellent private schools and made such adequate progress that both schools and family decided to transfer him at age 14 to public school. In the summer hiatus following this decision, Jimmy developed an acute psychotic reaction with all the classic Schneiderian signs which only partially remitted after a year of treatment.

Jimmy's biological vulnerability was obvious to all. In other instances, a biological vulnerability may exist, but because we lack any clear-cut vulnerability markers, we cannot evaluate its presence in any specific case. A biological vulnerability interacts sequentially and synergistically with the significant life events that transcend the developmental periods from infancy to late adolescence. Of all life events, those occurring within the matrix of the primary family group seem most significant. Congruent with the observations of Lidz, Fleck, and Cornelison (1965), we have found that the family relationships of preschizophrenics are notable for their disturbed patterns of communication, negative emotional climate, and deviant role structures. These aversive family relationships are incompatible with the growth of social competence and self-esteem in an already vulnerable person.

Once a schizophrenic reaction has occurred, the person undergoes a series of altered states which are often very uniform in character across persons. As suggested by Malcolm Bowers (1974), the phases of a psychotic breakdown follow a rough sequential order, terminating in the classic symptoms of schizophrenia as described in *DSM-III* (American Psychiatric Association 1980). This suggests that the underlying biological mechanisms are highly patterned and reflect a stereotyped functional disorganization of brain neurophysiology and biochemistry activated during a psychotic reaction. The major contribution of biological psychiatry to our understanding of schizophrenia has been to provide us with remarkable insights into the dysfunctional neurochemical patterns associated with the active phase of schizophrenia.

When remission from the active psychotic state occurs, and it mostly does to some degree nowadays, due largely to neuroleptic treatment, the patient is still highly vulnerable to a multiplicity of environmental events. This is particularly true at the present time as the periods of inpatient stay are extremely brief and the subsequent remissions highly tenuous. Because the released schizophrenic person frequently looks reasonably well put together at the time of release to the community, there is a strong tendency to underestimate vulnerability to relapse and to encourage premature reintegration into social and vocational life. The vulnerability of the postpsychotic state is similar to that of the prepsychotic state, only exaggerated by a factor of 100. To use a crude analogy, if the prepsychotic individual had an unusual sensitivity to sounds at the level of ordinary speech, then in the postpsychotic state even a whisper is excruciatingly disturbing. Maintenance pharmacotherapy can do much to reduce this vulnerability to environmental stimuli but is not sufficient to forestall relapse in over half of the cases. Once again, there appears to be a special sensitivity to attributes of the intrafamilial environment during this highly vulnerable period. Criticism, emotional overinvolvement, or premature pressures from significant others to resume normal role functions seem to enhance the likelihood of relapse with an active psychotic state. Just how these family attitudes and behaviors increase the vulnerability to the return of the psychotic state is not well understood, but it is increasingly clear that when family intervention programs support and encourage less pressure and a more benign emotional climate, relapse rate can be lowered significantly. Whether multimodal aftercare programs which combine pharmacotherapies and family therapies affect the longer term adaptation of the previously schizophrenic person is not known.

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A Dialogue Among Patients, Families, and Professionals—Editor's Introduction

by Richard R. J. Lewine

By 1979, the year in which the idea for a "consumer's" issue of the *Schizophrenia Bulletin* was first conceived, several major events and trends had begun to have a major impact on mental health care, especially for the chronically ill.

- "Deinstitutionalization" had resulted in a massive exodus of mental patients from long-term institutions to communities often unable or unwilling to care properly for them. "Psychiatric ghettos" had replaced "back wards" as the bane of the mental health system.
- A decline in the economy made it difficult to provide the resources desperately needed by the chronically ill and their families; the scarce resources that did exist were more likely to go to "good prognosis" patients than to the chronically ill.
- The psychiatric world had been undergoing what has been dubbed by some as a "neo-Kraepelinian" revolution, a return to a conceptualization of schizophrenia that emphasizes deterioration in functioning and a poor prognosis.
- There had been an explosion of "consumer awareness" and an increased critical examination of services and products in many different areas. What had been taken on faith, mostly in experts and authorities, was now held up to inspection, often resulting in consumer dissatisfaction.

The convergence of the above factors may be seen as having created a substantial group of people who were thrust into the role of primary caretaker of ill relatives; lacked adequate emotional, physical, and financial resources to do so; and were unwilling to accept their fate. As originally conceived, this issue of the *Bulletin* was to provide a forum for people of different backgrounds, views, and experiences to present their questions and critiques of the mental health system as currently implemented. The primary focus was on those who have been neglected, disenfranchised, or otherwise not satisfied with current mental health services. As we might expect, this led to the chronically mentally ill and their relatives.

With this goal in mind, ex-patients, families, and professionals interested in the plight of those with chronic mental illness were contacted and asked to contribute in whatever way they could in telling their stories and offering their suggestions. The response was, quite simply, overwhelming. The intensity and frequency of response were in themselves an important indication that the "consumer's" view was one that deserved public discussion.

I would like to extend my deepest thanks to all of those people who contributed directly or indirectly to this issue. Unfortunately, not all of the original contributions have been included; indeed only a fraction of them has. This is due, in part, to the ever present problem of space. More important, however, we have found that many of the articles were similar in content, an indication that being or caring for a chronically ill person has consequences that are common to many and may therefore have some common remedies.

This issue is divided into three sections: Ex-patients, Families,

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and Professionals. Marcia Lovejoy and Ronald Peterson, both ex-patients who have had a diagnosis of chronic schizophrenia, teach us in a dramatic way that labels are not the end point, even when those labels predict the worst outcome. Further, they serve as much needed success models for those with serious mental disability. Nevertheless, as we read their stories, we may well find ourselves questioning the "real" diagnosis, a reaction that may speak as much to our biases as to diagnostic error.

In the family section, Mary Jean Willis tells us of her personal battles in watching her son go from athlete, senior class president, Boy-of-the-Month, good student, and a happy, fun-loving person to one with recurrent psychotic periods during which he has tried to kill himself by sticking a knife in his stomach, cutting his throat, and running in front of cars—all in the presence of his family. Not only does serious mental illness have a tremendous emotional cost, but it also creates many practical problems, as presented in a survey of self-help groups by Holden and Lewine. They further echo the theme common to many that families of the mentally ill do not have the professional support they need to carry their burden successfully. Pringle and Pyke-Lees describe how dissatisfaction with professional help has led to the formation of the National Schizophrenia Fellowship (NSF), a self-help organization with a long history of successful work in family support, education, and political lobbying in Great Britain. The NSF was chosen to be represented in this issue since it was the first national organization of its kind and because it serves as a reminder that the issues to be raised are by no means specific to the United States.

Kayla Bernheim, a clinical psychologist, and Betty Nordwind, a lawyer, challenge their colleagues to reconsider traditional views about their roles in the mental health system. Bernheim offers "supportive family counseling," an orientation that emphasizes the family's needs and active intervention in meeting them, as an alternative to family therapy. Nordwind argues that the chronically mentally ill have not received adequate treatment and calls on lawyers interested in mental health to fight for changes in community care via the legal system. Both take a practical view of the sorts of help that the chronically mentally ill and their families need.

By 1979, when this issue of the *Bulletin* was proposed, another major event in the area of mental health services had taken place: the formation in the United States of the National Alliance for the Mentally Ill (NAMI). Over 100 family members, many of whom had formed local self-help groups, met in Madison, Wisconsin, to discuss the plight of persons with chronic mental illness and their families. The result of this convention was the formation of NAMI, a national organization devoted to improving mental health services through education, policy formation and political lobbying, support to families, support of research directed toward prevention and cure of serious mental illness, monitoring of ongoing mental health services, and the definition and defense of family rights.

In its short history, NAMI has already proven itself to be an effective organization, at local, state, and national levels. Its formation, conflicts, and successes parallel in many ways what this issue of the *Bulletin* is intended to do on a small scale:

- to bring together those with personal and professional contact with mental illness,
- to stimulate interaction and dialogue among diverse viewpoints that challenge us to rethink and reformulate our long-held beliefs,
- to inform each other, and
- ultimately, to form alliances that cut across professional and personal boundaries in our ongoing struggle with mental illness.

With these goals in mind, you are invited to read and respond.

Acknowledgments

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Expectations and the Recovery Process

by Marcia Lovejoy

Abstract

Personal experience is used to illustrate the effects of expectations on a patient's self-esteem and hope. The author, who was diagnosed as having chronic schizophrenia, points to the self-fulfilling nature of expecting a poor outcome. Project Overcome is one attempt to provide patients, families, mental health professionals, and the general public with models of successful patients. Former patients are available to lecture about their past experiences, thereby demonstrating through their actions that there is always hope.

Even a cursory examination of the current literature (see *Schizophrenia Bulletin*, Vol. 5, No. 3, 1979) reveals that the debate over the classification of various subtypes of schizophrenia still rages. Biochemical, genetic, and environmental theories compete with symptomatic categorizations, only to be challenged by premorbid case histories as the parameters within which schizophrenia is viewed. A primary goal of this search is prognosis, the discovery of predictive indicators that will enable clinicians to determine which clients can be expected to improve. The other, inevitable side of the coin is that they will also be able to predict which clients will probably not improve. And therein lies the danger of categorical labeling. The effects of such an emphasis, and its resulting expectations, upon the clients with the "wrong" (i.e., poor prognosis) subtype are immeasurably damaging, compounding the overwhelming social stigma clients face in attempting to overcome their illness.

I speak with some authority about the effects that professional expectations and community attitudes have upon the recovery process because my own label, since 1965, has been "chronic schizophrenic." And although I may not be qualified to speak about the etiology of my illness or the legitimacy of the various subtypes (e.g., chronic, paranoid, poor premorbid) under which that illness was classified, my experiences have taught me valuable lessons about the human consequences of such a self-fulfilling prophecy. I have also learned that there are ways in which clients and professionals can combat the stereotypes and accompanying hopelessness that stand in the way of recovery.

I began to hallucinate at the age of 9. My classmates quickly noticed that I was "different," and reacted to me "differently." Due to brain damage that would not be detected for another 17 years, my physical abilities lagged far behind those of other children. Simple skills such as balancing in hopscotch, catching a ball, or running into a twirling jumprope were extremely difficult for me. The more I tried and practiced at home, the more difficulty I experienced. My classmates ridiculed my efforts and I reacted to their rejection by isolating myself from them, knowing that I did not belong. I learned at an early age that I was not like other children, and that I must conceal my difference.

The 1950s were not an enlightened period, and my teachers saw my difference as the result of my being a recalcitrant daydreamer. I

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would giggle at odd times as I would "see" a troop of elves jump merrily from desk to desk and tweak the teacher's nose. At other times I would cry out at the sight of my desk biting my dress like a hungry animal. My behavior was annoying, and my explanations were seen as fanciful lies to cover up my disruptive behavior. When I was 12 years old, the family doctor prescribed medication for my "nerves." In high school, my mother gave me the phenobarbital that had been prescribed for her. By late adolescence I had learned that I could trust no one with the truth, and after two unsuccessful suicide attempts had decided stoically to see my life through to the bitter end.

My sophomore year of college was interrupted by increased hallucinations. I believed everyone was looking at me and I began sneaking down back stairways to avoid their piercing looks. I could hear the low growl of a tiger following me. Eventually I believed my room to be electronically monitored and that my thoughts were being recorded. Finally I was hospitalized.

In the hospital I was given medication, which ended the whirling in my head and banished the tiger's growl. I still feared others looking at me and I searched my room for hidden microphones. Even though I could not see them, I was sure the FBI was taking pictures of my every move. I was frightened: frightened of the FBI, frightened by others' critical gazes, and very frightened of this strange hospital.

The hospital itself was a kaleidoscope of images and emotions. Here were "sick" people dressed in street clothes, playing pool, and making billfolds. The rooms were large and clean, but the air was stale. There were no phones or televisions. There were a great many rules, which were not written anywhere, and apparently changed frequently. Receiving letters or telephone calls, and even private bathing were "privileges" that I must somehow earn. Being basically fearful already, I did well by quietly obeying everyone. I had seen what happened to those who did not conform to the rules. Several staff members would suddenly surround the offender with the phrase, "Are you going to cooperate, or do you want to go to 'South'?" South was the locked ward, and every day several patients were forcibly taken from my ward to South. Few returned from that ward, and those who did were unrecognizable. They did little but lie in bed, and when they walked, it was an odd, shuffling gait. Some even drooled. I was afraid of them, and of the staff, but my greatest fear was that this was where I belonged, and that this place would be my future.

My psychiatrist seemed pleasant enough, and smiled as he stopped by for a couple of minutes twice a week to sign my chart. When I inquired about returning to school, he cautioned me to dismiss the idea of ever returning to academic pressures. He said I should realize that I was ill and had to take things easy. I asked about looking for work, and he stressed that this too was out of the question for me. Maybe in a few months a volunteer job might be a possibility. He cautioned me not to think about any of these things right now, and just to regard myself as retired and needing a long, long rest. I would later learn that during this first hospitalization the doctors had decided that because of my long history of problems and the results of testing, I had a poor prognosis. My first diagnosis would be chronic schizophrenia. Although I had just turned 19, the professionals expected me to be a back ward patient, and advised my parents to find facilities that were custodial in nature.

I saw myself as incurably ill, as someone who would always need to be taken care of by others. My parents disagreed with the doctor's recommendations and urged me to change doctors. The second and third doctors, however, said the same things. I left the hospital and tried to fit into my new role as sick and retired from active living, but I was overwhelmed by the emptiness of my future. I became increasingly afraid of myself and my feelings, which doctors said were further symptoms of my mysterious illness. Because I was sick, my feelings and perceptions could not be trusted by anyone, even myself. The weekly visits to my psychiatrist were only so he could watch me become sicker, and prescribe more medications, or hospitalize me for the safety of the community. I felt ashamed, helpless, useless, and frightened.

My experiences in the community only confirmed these feelings. At a bus stop once, I struck up a conversation with a woman. The inevitable question arose: "What do you do?" I hesitated, but finally said that I was "retired" and that I had been in a psychiatric hospital. The woman's reaction was immediate and unforgettable. She gasped, then looked quickly for an approaching bus; seeing none, she flagged down a passing cab. I tried getting a job and painfully discov-

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ered the discrimination that surrounds mental illness. I eventually learned to lie and was hired. Applying for jobs far below my skills and intelligence, and fearful of discovery, I would become nervous and sleepless. If I complained to my doctor about my problems at work, he would suggest that perhaps I was not yet ready for work. If I then argued to continue working, he would increase my medication, and I would suffer from blurred vision and sleepiness, further compounding my work problem. If I hid my problems from the doctor and just kept them to myself, I also became worse. There seemed to be no solution. But I had to keep trying; at home, all I could do was watch myself and the hurt in my parents' eyes.

I had more hospitalizations. Most of them seemed the same. My life would go out of control and the doctor would suggest that I take a rest in the hospital. After the increased medication and sleep eased the roar in my head and I knew what was going on around me, I felt a deep sense of shame and failure. I spoke to a parade of doctors, nurses, psychology technicians, aides, and students, all of whom would ask me the same questions about my life and then jot notes in my chart. I would always be given the same advice: take your medications, follow the routine, and cooperate. I learned to measure my progress by external criteria, such as medication. If I was given less, I was doing better; if I received more, I was not doing well. Although I tried day treatment programs, medications, shock treatments, and hundreds of hours of one-to-one therapy with my doctors, nothing helped me to gain any more control over my life. No matter what combination of drugs, work, school, and therapy I tried, it would fail.

Some staff members did really try to help and would honestly offer advice or criticism. It was usually as a result of their friendship that I gained the courage to attempt a new job or to believe that I could really change and gain control of my life. There were always a few hospital or program staff members who helped me to try once again. However, the vast majority only succeeded in confirming my distrust of people and my feelings of worthlessness and hopelessness. The use of power which makes it possible for a handful of staff members to manage a ward also creates powerless victims, devoid of courage and self-respect. Power games create winners and losers; I was a loser.

The one comforting aspect of the hospital was my fellow patients. After I gave up the idea that they were the FBI in disguise, I found some companionship. At least it was easier to talk to them than to my doctors, nurses, or parents. Other patients especially understood my sense of shame, anger, and fear. Staff members always discouraged friendship between patients, saying that we were reinforcing each others' illnesses. They did not understand that we were also giving each other support and help. I could not confide my problems with hallucinations, or my fears about the FBI, to anyone who had not had similar experiences. Although it helped to share experiences with others who genuinely understood, there were answers we could not give each other: how to overcome it all; how to make it on the outside. We were all losers.

In 1972 I happened to end up in a drug and alcohol treatment unit. There I was treated quite differently. Staff members would be angry or smile because they honestly felt bad or good toward me, not for therapeutic reasons. They inspired me with the idea that I was responsible for changing my life, and that I could be sane in a crazy world, just as alcoholics could learn to stay sober in a drinking world. It would take time and effort, but it was possible. In this program, for the first time, I learned some things I could do to cope with living. Staff members called these ways of handling problems "tools." My tools would be unique for me as they needed to be individualized to fit each person's needs. I began to learn. I learned that I needed to be more than a passive, cooperative patient to recover. Now I had to find answers and people who offered more substantial help than before.

There were more hospitalizations and more symptoms. The hallucinations, fears, and suspicions alternated with periods in which I believed that I was dead and with periods of sudden, unpredictable, unpremeditated behavior that would surprise me as much as it did others. My doctor began to talk about a more secure environment; he meant the state security hospital for the mentally ill and insane. During the commitment process, I was sent to an interview at a halfway house. Although the halfway house accepted me, the hospital staff members believed that I needed a more structured environment. It was my good fortune that my funding ran out at that point and the staff members, having no alternative easily available, discharged me to the halfway house.

The halfway house changed my life. First of all, I discovered that some of the staff members had once been clients in the program! That one single fact offered me hope. For the first time, I saw proof that a program could help someone, that it was possible to regain control over one's life and become independent. The house was democratically run; all residents had one vote and the staff members, outnumbered 5 to 22, could not make rules or even discharge a client from the program without majority sentiment. There was a house bill of rights that was strictly observed by all. We helped one another and gave support. When residents were in a crisis, no staff member hustled them off or increased their medication to calm them down. Residents could cry, be comforted and hugged until a solution could be found, or until they accepted that it was okay to feel bad. Even anger was an acceptable feeling that did not have to be feared, but could be expressed and turned into constructive energy. If you disliked some aspect of the program or the behavior of a staff member, you could change things rather than passively accept what was happening. Choices were real, and failure and success were accepted equally. Although I was incredibly suspicious, I could find little about which to be "paranoid." I could read my file at any time. All problems were discussed at house meetings, so nothing was kept secret. Bit by bit, my distrust faltered and the fears lessened. I slept better and made friends. I was treated with respect and respected others, so gradually I began to respect myself. My life became more manageable as I learned the "tools" I needed. I learned about stress, how to recognize symptoms of stress in my life, and how to control or cope with the stressors. Other residents and staff members who had hallucinated for years and now were able to control their hallucinations shared with me some of the techniques that had worked for them. Things like diet, bioenergetic "grounding," and interpersonal relationships became a few of my tools.

Since that 18-month experience in the halfway house, I finally have been able to live a full and happy life. After 10 hospitalizations over the course of 12 years of treatment, I have finally learned how to survive, and have not seen the inside of a psychiatric hospital for 4½ years. But although I now feel that my life is under control, I know that thousands of others have not been so lucky and are still facing the same struggles with mental illness that I fought for most of my life. My experiences, as well as the experiences of others from the halfway house, have taught me that regardless of the cause(s) of mental illness, progress toward recovery cannot occur when there is no hope. Negative expectations and stereotyping are among the greatest obstacles to recovery, and keep many mentally ill persons immobilized by defeat and despair. It was to combat this climate of hopelessness that I initiated Project Overcome in 1977. Believing that the lack of visible, successful former patients contributes to the negative expectations held by professionals, community members, and patients themselves, I formed a speakers' bureau of men and women willing to speak publicly about their successful battles to control their own mental illness. Originally supported by a grant from the Minnesota Department of Public Welfare (the first client-run program ever to receive such a grant), Project Overcome now receives private foundation support to send its speakers to speak to parents, mental health professionals, and communities statewide. The intent and message of Project Overcome is one of hope: hope for others who may never have seen someone who has "been there and back." Project Overcome speakers share their experiences and what they have learned about recovery with patients in hospitals and community programs. They reinforce the idea that having problems is nothing of which to be ashamed—it is something to be overcome. We promote openness, risk taking, consumerism, and the assumption of responsibility for acquiring needed tools. We are living proof that it is possible to make dramatic changes in one's life, despite the worst expectations of mental health professionals, family, and the community.

Project speakers also offer hope and a challenge to mental health professionals, who rarely hear from their successful clients. These doctors, social workers, nurses, and others can play an invaluable role in helping people regain control of their lives, but only if they are willing to listen to their clients, their problems, and to help them to acquire the individual survival skills necessary to cope with life and its many stresses. In particular, professionals need to guard against limiting their patients' hope and participation. It is essential to see each person as a unique individual rather than a diagnostic category. Hiring former patients and using their advice to develop and plan treatment programs and to teach survival skills is one way that professionals could enrich current programs. The value of former patients as treatment program staff members has long been recognized in areas such as the treatment of alcoholism. It is time for the mental health field to acknowledge its participants.

Last of all, Project Overcome speaks to churches, schools, and community groups, dispelling the media stereotypes of the mentally ill as dangerous and incurable. Audiences typically ask, for the first time, all those questions they had always wondered in secret. What is it like to hallucinate? What is it like to receive shock treatment? The facts are always surprising. We are not only like you, we *are* you—your sons, daughters, husbands, sisters, and fathers. We need jobs, housing, a chance to become independent, and accepted. We need to learn from and support each other. We need the same respect and freedom that you value and we have much to contribute to our communities and to the mental health field.

The time has come to go beyond the categorizations, the old images, and the destructive expectations. Our hope lies in hope: creating a climate of support, learning, and encouragement for those who seem to have no reasons left for hope.

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Schizophrenia Bulletin Index 1969/79

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What Are the Needs of Chronic Mental Patients?

by Ronald Peterson

Abstract

A former long-term resident of a state psychiatric hospital describes the obstacles to successful re-entry into the community. Among the problems facing chronic mental patients in the community are housing, loneliness, absence of choice, lack of meaningful activity, and unrealistic expectations of others. Fountain House, a clubhouse model program, run by its members and staff, provides the emotional and practical support necessary for patients to become a contributing part of the general community.

I think I ought to tell you a bit about myself. My name is Ronald Peterson and I'm 29 years old. I was asked to write this article because I spent quite a few years in a mental hospital. I don't remember all of it too well, but I went to the hospital when I was around 8 years old, up at Rockland State, and I stayed there for almost 10 years, including the 2 years I was at Pilgrim State.

I've thought about what my diagnosis could have been. I think they would write in my record a lot of the same things which other kids were doing. I got Thorazine which brought me down when I was too high, getting into mischief, and tearing off my clothes. I don't know what the diagnosis would be, but I'm sure that there's a name for my kind of behavior, and someone said it was schizophrenia.

I was about 19 when they asked if I wanted to leave the hospital and come back to New York City where I was born. When you leave the hospital, one of the most important things you have to think about is where you're going to live. In my case, I had no home to go back to. They got me on welfare and in a small hotel room on Times Square. I'd get my check at the desk and sign in. The clerk would take out the rent money and I'd do this twice a month.

You don't have much left over to live on when you're in a single room occupancy—an SRO—and you don't get much space to live in for the money you pay. When you're all by yourself, you can feel really lonely, even though you can see lots of people on the streets. But you're still isolated and by yourself. Most of all, you aren't living in a place you chose for yourself. It was simply arranged for you.

I realize you have to have a place to live when you leave the hospital, and they take what they can find. But I hope that younger patients like myself, and also the older ones, will have more of a choice or a chance when they leave the hospital. I know now that people like me don't always have to go to an SRO. Many of us, with just a little help, could live with each other in a real apartment of our own. This way we could have a bedroom, a living room, our own toilet, not one way down the hallway, and also a little kitchen where we could do some cooking if we wanted.

Most patients just don't go out and sign leases. They don't have money for deposits and all of those

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things. When you have no job, are on welfare, have no references, no money, and, most of all, no one to live with, you don't think about having your own place. It's just not something you even think about. You take what you get. But it really doesn't have to be this way.

Since 1957, we at Fountain House have had apartments for our members. Most are in the neighborhood, so you can save on subway fares. We hold the leases and the members pay us their share of the rent. By living together, members get more for their money, and in lots of ways they can help each other. We furnish the apartments with all the things we get at our thrift shop.

The members can stay in the apartments as long as they want. They can even take over the lease from us if they want to. There's no rule that they have to move on, and I think it's about time they have the chance to feel this way.

We now have some 60 apartments, and we need to get a new one about every month. Living in an apartment is a lot different from living in an SRO, and I hope that all patients leaving the hospital can be guaranteed to have the chance to have a real apartment, a place they can call their own.

Even if we do the best we can, as to where a patient is going to live, that's really only the beginning. For example, what's going to happen when you get up in the morning, unless you spend a lot of time sleeping, getting up late, just walking around, hanging around the streets, doing nothing? Some of us, of course, can go back to jobs we had, or get new ones. But many of us can't do this, and I think the greatest need is to have a place to go, where you are expected each day, a place where you can be with people like yourself, and do things that mean something.

At Fountain House and some other places I've visited, we are able to do all kinds of worthwhile, needed things, 5 days a week. We can visit our fellow patients who are not coming in, because this can happen to all of us at times. And when we knock on the door, we're not told to go away. Almost always we're welcome, and this helps to get somebody back into things. We go to the store and buy food for lunch, cook and serve it, and we do a good job cleaning up afterwards. We do all kinds of things in the daytime at Fountain House. We start at 9 o'clock in the morning and finish up around 4 o'clock in the afternoon. The 400 members in our prevocational day program made a long list of the things we do, and here are the first 50 or so things they mentioned.

> We eat, have coffee, sit and talk with each other. We type, wash clothes, cook and sew. We go to the A & P store, run the cash register, take showers, vacuum and dust, tutor our fellow members, and run the snack bar.
>
> We conduct tours every day for visitors, welcome fellow members at the front door, serve customers in our thrift shop, prepare our daily newspaper, and wait on tables at lunchtime. We check coats, add and subtract, wash dishes, operate the copying machine, and take the mail to the post office.
>
> We file, fix up apartments, dictate our rehabilitation plans, interview new members, orient them to Fountain House, and operate our audio-visual equipment. We take dictation, run the offset machine, help with accounting records, price merchandise at the thrift shop, and present the daily news on television. We visit members in the hospital, write articles, help members get on welfare and S.S.I., and are part of the faculty for our NIMH training program. We reach out to drop-outs, go to work on transitional employment placements, and help train our replacements when the job placement is about over.

Our clubhouse is a busy place, but you have to remember that many of us did do a lot of things in the hospital. If given a chance, we can do lots of things in the community—if we have places to go to and can be with people who need us to contribute, to take part, to help, and who notice when we're not present, and who do something about it.

I think the word "opportunity" describes what I'm trying to say. For me, it meant a lot, after being in the Fountain House day program, to have a chance to try a job, a real one, which I would never have gotten on my own. It was hard to believe it was true. I didn't have a good job history. I didn't have any at all, except for the job I was fired from, and that's no way to apply for a new job. I didn't have much education, and being a mental patient in a big institution for most of your life doesn't help a boss want to hire you.

I was on welfare and I don't think this ever helps. And things like references—I didn't have any, except for a social worker who kind of liked me. I'm not sure I would have done very well in the job interview. I would do all right now, but back then it was different.

Yet, I had a chance to go to work on transitional employment because none of these things counted. You might say I had the chance to work because of all the things I lacked. After a year or so of doing lots of activities at Fountain House, going on my first job placement for 4 hours a day wasn't too hard. I went with a group of fellow members to a Chock Full O' Nuts Store, down on 7th Avenue and 28th Street, and we did there most of the things we were doing at Fountain House in our dining room, and in our snack bar.

But it was a regular job, in a real restaurant, and all of us got the regular pay. We were all mental patients, vocationally disabled, on welfare, but we knew we did real things at Fountain House and it wasn't that much different on a regular job. Most of us did okay. Even for those who didn't, it was all right, because they came back to our day program and it wasn't like losing a job and having no place to go. We might have felt a little bit that it was a failure, but we looked at it as a big step anyway, in trying to get more on our own.

If you have the chance to go to work without having to pass lots of hurdles first, you discover things. All of us found that we could do parts of the job very well, but couldn't do so well on certain other things, so we learned to be of help to each other. In time, we didn't have to help each other so much.

Each day, over 120 of our members go to work on job placements in some 40 business firms in New York City. They work 4 hours a day, so one job can be used by two members. They get the regular rate of pay and earn over $300,000 a year. Some 29 programs elsewhere in the United States have now started similar programs. Altogether, almost 475 patients are going to work in over 160 business firms all over the country, as part of their rehabilitation, and with earnings of $1,300,000 a year.

But it's not all success. We need the chance to fail, as long as we still want to keep trying. Maybe some day, what needs to be done for us can be done quickly, but I don't think we've gotten to that point yet. I think what we need now for those of us who are looked at as severely disabled are places in the community where we can keep coming over a long period of time, a year or two, or even longer for those who need it.

One of my co-workers at Fountain House, a social worker, said something one day about his two children who had just finished college. He said he didn't see too much difference in them after 4 years of college, at a cost of a lot of money. I liked what he said because it also referred to me and my fellow members who are at Fountain House and at other places like ours across the nation.

How quickly then do we have to change, to be trained, to live independently in the community, to be treated, to no longer be chronic, to no longer be socially and vocationally disabled? We have had an illness not yet understood, and we have had all kinds of medical treatments through the years. Many of us have had many hospitalizations, or spent many years in mental institutions. Our lives have been influenced by these experiences, quite aside from whatever our illness has done to us.

We need, therefore, to be with others who believe that we are not at our best, and that sufficient time will be given us to be at our best.

One way to help us continue to fail is to expect a kind of miracle, an almost instant change. Or to believe that we can never change and will always need to be dependent.

Maybe if we all could become little again, it would be easier for everyone to solve the problem. I don't mean that we're children, but I'm thinking about a family and what seems to go on there. In a family you really don't feel you're being "raised," that people are doing things to you, to raise you. Your life seems "real," and you can talk about almost everything that happens to you. Sometimes you have good news, sometimes you have bad news. But most of the time, it's just talking about what is going on.

It's a place you go from, to the doctor or to the hospital or the dentist, or to school, or to the movies or to a job. But it's a place where you belong, where you somehow learn a lot. You change, I'm sure, but usually without knowing it. And you certainly are not looked at as a patient, or one who is being rehabilitated. You don't get discharged or terminated, and even when you grow up and get a job of your own and move away, it's a place you keep in touch with and visit. There's always an interest, and that's what makes the difference.

I think this is what we need for the chronic patient. We don't have such places in our lives, and while we can't be little again and go back to small families, we ought to have, whenever there are enough of us around, a kind of bigger family where you don't feel you're a patient—that someone is doing something to you for your own good, where no one would say "that's not my department, that's not my job, that's not my problem." In a place where you do things together, there's a common interest in almost anything that's happening to you.

I hope some day you will come and visit where I work, and talk to as many members as you would like. I would like to show you the snack bar and have you meet the members I work with. Most of them are younger patients from 16 to 25 years of age. I would like you to visit some of their apartments, and I would like you to visit some of the jobs they are working on in transitional employment. There's Gladys, for instance, who spent years in the hospital the way I did and came to Fountain House when she was 16. She got her first job in her life at Sears, just before she turned 17. You could see all the things we do in the day program, getting ready to go to work, and you could sit with us at our daily meetings.

Our members will be glad to talk about what they think is needed. First, they need a place where they can get their lives started again:

> You can't get anywhere unless you first get established. . . . It's simple, it's like having a bottom to one's life. . . . It's a start, that's what it is. It's a place where you get your life moving again.

Having no place to go and feeling lonely and isolated was described again and again:

> When you're alone and doing nothing, you feel more nervous. . . . I used to spend all my time staying in my room. . . . When I stay at home, I get sicker. . . . Just coming here, that's what counted, not being alone all the time. . . . Keeping busy and having things to do is very important. . . . I've got a lot of work to do here every day and this makes me feel worthwhile. . . . Here there's no busy work—everything we do is something that has to be done.

All of our members have abilities which are needed, and the chance to develop their own skills is very meaningful:

> I have learned I can do a good job. . . . I have learned to do paper work again. . . .I've kept up my secretarial skills. . . . Most of us discover talents we never thought we had.

Their comments about being needed help to explain why the chronic patient in the community needs a special place to relate to:

> Here you are really needed. . . . This is the only place in the city that can use me. . . . I'm expected here every day and that's what is important to all of us.

As to our apartment program and the chance to live with fellow patients:

> I got a nice apartment instead of a lonely, dreary room. . . . I was alone in a welfare hotel. . . . Now I have an apartment and a roommate. . . . I was still in the hospital when they got an apartment for me.

The chance to have a job is most important:

> I never worked before and now I have a job. . . . Everyone needs a chance to go to work. . . . They gave me a job while I was still in the hospital. . . . I'm starting my job a week from today. . . . This is what counts, to work and have a chance to make some money.

The chronic patient needs a place in the community which he feels helps him stay out of the hospital, or to get out of the hospital:

> Being here has helped me stay out of all the hospitals where I have been in the past. . . . Being here is so much better than going back to the hospital. . . . Here they help you get out of the hospital and stay out of the hospital. . . . I come here every day now and I believe it's cutting my time in the hospital.

Our members need to have a sense of future and look forward to more independence:

> It's really something to feel you are back in the world today. . . . I feel more adjusted to the outside world. . . . For the first time, I'm looking forward to the future. . . . What you get here most is hope for the future. . . . Here we have the outlook that all of us can make it on our own some day. . . . I'm 30, and it's about time to get away and be on my own, to live my own life.

I believe that chronic mental patients become less chronic when they are in a place they can feel good about. There are lots of complaints and gripes, as in all big families, but they also have a lot of good things to say:

> I feel good being here. . . . This is my second home. . . . I enjoy it immensely most of the time. . . . It's a pleasure for me to be here.

As you would expect, many mental patients have uncomfortable and distressing feelings which need to be reduced, and they need a place where they can feel better:

> When I feel insecure, I come here and it helps. . . . Here I discover again and again that I'm not such a bad person. . . . Here I don't feel so afraid. . . . I come here because I don't always feel human. . . . It's simple, being here helps me feel better. We feel more confidence in ourselves here. . . . It's helped me to try again . . . to feel more grown up . . . to feel more self-reliant.

Chronic patients in the community have a need for other people, to talk with, to do things with, and just to be themselves with:

> The best thing here is that it gets us together. . . . Being with others, that's what helps. . . . Most people don't appreciate what people can mean to each other, that you are important to them, not just to yourself. . . . I'm not so afraid to be with people any more. . . . It's simple, here we get back to the world of people again.

When you have a place in the community that you like to come to, feel a part of, and can participate in, you can help yourself by helping others:

> We're being helped by helping each other. . . . Here you help others and this is how you help yourself. . . . We need each other, to help each other.

I wish that everyone who believes that chronic patients are totally chronic could see all the things our members do each day and hear all of the things they have to say. Some day, I hope we'll have a book of what they think, and then people can be more hopeful and not use the word "chronic" for anybody, at least until we have given them opportunities they and all people need.

I know from my own experience that this is not done too much in the hospital, and I know that we're still not doing too much about it for all the patients in New York City. My interest is the younger patient. Most will not grow up in a hospital the way I did, or will not spend lots of years in the hospital as so many of the older members at Fountain House did. But they can still become disabled in the community, unless we do what needs to be done.

I believe that our chronic patients really don't need as much as we think they do. What I'm trying to say is that I think we haven't done much for lots of people, and they have lots of needs. But if we start doing something about their needs, I think we will find we really don't have to do too much.

As you know, I'm not a professional. It's hard for me to decide certain things that I hear others talking about. For example, are members who do well at Fountain House really chronic? Some visitors say that patients they have back home are too sick to do what we do. Other visitors who come to our Monday night dinner meetings and listen to our members who have full-time jobs say that they are not chronic patients. Some visitors have the same idea about our members who go to work each day on transitional employment placements.

I don't know for sure what you have to be to be chronic. I was in the hospital for a long time, and I don't know if I was chronic or not. I don't know for sure for any members of Fountain House.

At our meetings, members take turns talking and my fellow member, Cora, had this to say:

> Well, I'm going to tell my age. Okay, I'm 28 years old. I'm a dictaphone secretary at a big textile company in Manhattan. I make $185 a week. I go to school 2 nights a week and I'm studying to be a court reporter. I have my own apartment, I have a cat, I have a boyfriend, I have a driver's license, and I have a piano, and that's now.
>
> I'm very happy and I feel very healthy. And when I came here tonight, I felt that it was very important to come to a place where I've always been made to feel special.
>
> I came here 10 years ago when I was 18 years old. I had a small little tiny room in the YWCA. I had no job, and I collected money from welfare, which gave me about $2 a day to live on. I was very, very nervous, and very, very frightened.
>
> I had spent about 2 years in a state hospital, and I guess I had every course of treatment—tranquilizers, shock, and all of that. Somehow when I left, I felt worse than when I started. It's almost as if you feel that your brain is straw. But somehow or other, I came here to Fountain House.
>
> Fountain House is a very large place. There are a lot of different areas to work in. I worked in clerical and in the snack bar, and I have been on job placements. Fountain House even sent me back to school, and then got me into college, where I got my high school equivalency. By then I was about 24 years old. I had had another hospitalization when I was 21, but I came back to Fountain House—I get kind of dizzy thinking back.
>
> I had a lot of transitional employment. A lot of part-time jobs. It's like going to school—like going from the second grade to the third grade to the fourth. You don't know what to expect, but it's like graduating in a way. It's not that each new job is necessarily much easier, but it's like learning something.
>
> I had a lot of friends when I was here. I had a whole social group and I used to love to come here, not only for socializing and things like that, but it filled a lot of time up. I didn't have much contact with my relatives. I had no friends from before my first hospitalization. Everything that I did was here.
>
> I had two jobs before this one: I had the one that I quit, and the one that I got fired from. Then I got this one, and I've been on this job for 19 months. I've gotten one raise already. It's a very nice job, and I'm going to

> school, because I think that I'm capable of earning more money. About 3 years ago, I got an apartment.
>
> I don't know, I came here tonight and I spoke to somebody, and I tried to get the feelings of what it was like before. I remember being terribly afraid of a full-time job. I mean they would tell you about full-time jobs, and it was the one thing I really didn't want. I was worried about my $2 a day on welfare, afraid to risk a full-time job. Now, it amazes me that I felt that way. This is the first summer that I'm keeping cool by my own air conditioner that I saved my own money to buy.
>
> I would never have known 10 years ago that things would have been this way. Maybe 10 years ago, I would have wanted them somewhere else. But right now, I am very happy with the way it turned out. I mean, it's almost a miracle as far as I'm concerned.
>
> And most of it is due to Fountain House, because all I can think of is that if Fountain House hadn't existed at that time, giving me all the moral support—well, I feel that I came to visit a very wonderful relative when I came here tonight. I really don't think I could have made it, because I did not have that much health or that much strength 10 years ago, to talk myself through depressions or feelings of fear and disappointment.
>
> I've seen bad things happen to people and I've seen good things happen, but nowhere is there a place where you get so much support. No other organization that I know of gives you so much guidance or faith. It's like a secret thing I learned from Fountain House. I was at work today and I knew I was coming to this dinner tonight, and I know that to me this dinner's very important, but I'm not going to tell anybody I'm coming here.
>
> Would you like to ask me some questions? I feel that I'm babbling.

I also want to share with you what another of our members had to say, and I hope the words of our members will help you to want to set up places in the community so that more men and women will have similar things to say in the future about their lives.

> I'm a clerk for the City. I make corrections on work that goes into the computer in the keypunch area. If they punch errors, I'll correct them. The job pays well. It doesn't require complex clerical skills, but you have to think and use your head to a certain extent.
>
> I've been working since November 1973. Previous to that I worked a year on a job placement as a full-time messenger. I've been in the hospital for 10 years straight. If you want to know why the hospital didn't work and Fountain House did—this is my own theory.
>
> People will behave according to their surroundings. In other words, if you go to another country, you will adapt to that country. Now you take anybody, put him in an institution, call him a patient, put him in bed, treat him like—I don't know—something in a ministerial level, doing everything to make him feel sick, well, after a while he's going to start believing it, whether it's true or not.
>
> Even if you're well, you can get sick in a hospital. And if you're sick, you can get sicker. And when you come out of the hospital into Fountain House, you find there are really no technical brilliances at Fountain House. There's no complex Freudian theory or anything like that. It's just a common sense approach. You call him a member, not a patient. You come to a very beautiful building, a modern building. You start out working to a limited extent.
>
> When you're out of a hospital, you can't do a job like mine. I couldn't do it when I first started out. Here they treat you as a person, not as a patient. You start out when you're ready for it on a simple job—carrying messages, collating—very simple jobs for 20 hours a week. You progress slowly, gradually, to more and more. You may start working full-time in a simple job, or you may go to school to learn a skill, or you may work part-time and go to school. Eventually, you get set up on what you're capable of doing, whatever that may be.

It is my hope that you will believe, or allow for the possibility, that these two fellow members of mine, including myself, were chronic patients or could have become chronic. If we in the mental health field cannot do this, then there's no hope. It would mean that we are helpless with chronic patients, are without fault, and can't be blamed in any way for chronic behavior, either in the hospital or in the community. But if we accept responsibility for chronicity, I think there will be far fewer chronic patients among us.

As I have said, I grew up in a mental hospital and spent 10 years of my life there. I was also a patient in the community, where things did not go well for me, and I failed. And I spent 3 years trying to get my life together, which I think I did, and for some 6 years I have been on the staff, working with people pretty much the way I was years ago.

Most are young. Some are educated, not like me. A few are Puerto Rican, some are white, and some, like me, are black. I think it's harder, if you are mentally ill, to be also poor, uneducated, and from a minority group.

I say this because we really have

the same job to do for the disabled, or mentally ill, as we have to do for those who become disabled because of race, poor education, and poverty. The job can only be done if we who are disabled have the main job in overcoming the disability. The society in which we live has to give us the places we need to overcome our disability, which is not just due only to our illness, any more than it is to color or whatever else you may choose.

I was not into the civil rights movement in any active way. But when I came out of the hospital, I saw a lot on television, and in certain ways there is a connection between what happens to a lot of black people, or other minority groups, and what happens to patients in the mental health field.

It might be a good idea, to help things get better, to have patients in good places transfer for a while to places where things haven't gotten started yet. If you're a patient in New York, or in California, you can be a patient anywhere.

Maybe some day patients can be a part of a training program where some can transfer to other settings that need assistance. I don't mean by working with the staff so much, but working with the fellow patients who are out there in cities across the country.

I recently went to the State of Maine for the first time in my life. I made a site visit to a mental health facility in Bangor and to a state hospital in Augusta. Like other staff at Fountain House, I spend part of my time in our training program where people from across the country come for 3 weeks to experience what we are doing. This helps them to set up similar services in their own communities when they get back.

I've met and talked with, and helped to train, a lot of the people who come to us, and I think good things are beginning to happen for chronic mental patients elsewhere in the country.

To finish up, I have tried to say lots of things about what we need as chronic patients in the community. Most important is to stop looking at us as chronic. We can be helpful to each other. We can learn from each other. We can set examples for each other, and we can encourage and support each other. Somehow, we know that each of us can do better. When we get this message across to each other, we can change, and do more with our lives.

I have tried to talk about the housing we need, the chance to work on real jobs, and most of all, a place in the community where our being present is not based on what's wrong with us, but rather on what is right with us, to contribute, a place where people believe in our being able to do a better job, where the opportunities we need come together in one place.

We need to go to doctors at times, like everyone, and to hospitals, to high school and college, to jobs of our own, to our own apartments, and to go on vacations, and to live in other cities, just as everyone else does. To do this, we need a place which somehow has been absent in our lives. The hospital was not that place. If we can have these places, you will see that most of us are not so disabled as we appear. These places will let us be there when we have to, and also help move us on to whatever we are capable of doing.

The Author

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The Impact of Schizophrenia on Families: One Mother's Point of View

by Mary Jean Willis

Abstract

The practical consequences of deinstitutionalization upon the families of the mentally ill are discussed. Not only is adequate care frequently lacking for the ill family member, but the families of the mentally ill often find themselves alone in their caretaking roles. The growing importance of consumer-advocacy groups may be a harbinger of increasing cooperation among all those concerned with the impact of schizophrenia on both affected individuals and their families.

When my mother-in-law's youngest son became schizophrenic back in 1941, and was committed at age 18 to a mental institution where he still remains (that is the way it was done in those days), and my mother lost her only son in a training-mission plane collision 6 years later, I thought then (and still do) that of the two tragedies, my mother-in-law's was the worst. At least my mother felt no guilt about what happened to her son; she could talk about him to her friends with pride, and she knew he was at peace and had died doing what he loved. My mother-in-law, on the other hand, never spoke of her "put-away" son, and in the beginning when friends and relatives asked about him, vague answers were given, and the subject quickly changed. In the end, he was forgotten by all but his closest family members, and became a sort of nonperson, one of the "living dead." Never did I imagine then that 30 years later my husband and I would hear the same dread word "schizophrenia" applied to our own dearly beloved youngest son. But things are different now than they were when my young brother-in-law was sent away to live out his days in the dreary confines of a state mental hospital. Now we have "deinstitutionalization," release of the mentally ill from hospitals as soon as they are stabilized (and sometimes even sooner).

We think that our son was prematurely discharged from hospitals at least twice. At one time he was sent home on a weekend pass from a state hospital. When the family, including our older son, daughter-in-law, and their infant daughter, was gathered together to celebrate his homecoming, he suddenly disappeared into his room where he proceeded to smash a glass and slash at his throat. Another time, when he was hospitalized in San Francisco after throwing himself in front of a car, he refused medication and demanded to be released. The hospital would not keep him against his will, so he was discharged after a few days, whereupon he jumped in front of a truck and was severely injured.

Deinstitutionalization has meant not only early discharge, but also inaccessibility of hospitals. Because our son is suicidal, we have not had any great difficulty getting him into a hospital. However, I know of a mother who has not been able to gain hospital admission for her son, even though he is violent and a danger to society when he is in his manic phase.

In the 10 years that our son has been a diagnosed paranoid schizo-

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phrenic, he has been in and out of hospitals, both private and state, in Colorado, Hawaii, and California. He has lived in halfway and three-quarter-way houses, and has been treated by private psychiatrists and mental health therapists. He has made many suicide attempts, and he chewed off part of his tongue in a frenzy when he was strapped down in both a private and a state hospital. He still retains a wry sense of humor and a consideration for others in spite of all the suffering he has gone through. We enjoy his company during the times when medication has stabilized his illness. But the stress we are under during the frequent periods when he is "decompensating" at times becomes almost unendurable.

It is very difficult to cope with our son's manic, irrational, paranoid behavior (with suicide attempts such as sticking a knife into his abdomen, cutting his throat, running in front of cars—all done in our presence). At such times we desperately need professional help in handling these crises—in getting him calmed down, persuading him to take more medication, or go to the hospital. We are fortunate now to be able to turn to his mental health center therapist for assistance, but in the past we did not always receive such help from his private psychiatrists.

When we are forced to manage by ourselves, we try to remain as calm and loving as possible. If our son is not completely out of control, we are sometimes able to persuade him to hike with us in the foothills around our home, or my husband might play pingpong with him, which often seems to have a calming effect. We find it best not to try to argue with him about his paranoid delusions, but to try to keep the conversation (such as it is) on a light and cheerful note. If hospitalization is necessary, we are sometimes able to get him to let us take him to the hospital. At other times, nothing we say has any effect, and then the only alternative is to call the police.

The deep sadness of such a blighted life (a former athlete, senior class president, Boy-of-the-Month, good student, and most important, a happy, loving person) doesn't bear thinking about. We must constantly fight with ourselves not be become bitter, guilt-ridden, and full of self-pity. In the last 2 years I have found a constructive activity which has helped me to deal with this tragedy. When I at last faced the fact that our son might not get better (unless there should be a miraculous breakthrough in attempts to find the cure of schizophrenia), I began to "come out of the closet" and to think about forming a mutual support/advocacy group. I felt that so much needed to be done for the chronic mentally ill that those of us who are the most deeply involved with them—their families—must band together to help them and to help ourselves. It so happened that two therapists from the Boulder County Mental Health Center, Boulder, Colorado, had also been thinking along these same lines. Eventually we got together and organized Families and Friends of the Adult Mentally Ill (FFAMI) for the purpose of helping families cope with mental illness by means of education and support.

At first I was reluctant to come all the way "out of the closet" and have my name appear in the local papers in articles about our group because our son had indicated his displeasure at my being involved in such an activity (he usually will not admit that he is mentally ill). Other members also felt this way, but we finally decided that if FFAMI was going to succeed, it was necessary to publicize it. So we consented to giving interviews, and articles appeared in two newspapers which engendered much interest in our group, and were mainly responsible for a dramatic increase in our membership. No harm was done as far as our son was concerned, since he apparently did not read the articles.

FFAMI is almost 2 years old now and has begun to realize some of its goals. In cooperation with the Mental Health Center, a series of educational lectures is offered twice a year for the benefit of the families. In addition to the lecture series, educational and problem-sharing meetings are held each month. Members of FFAMI, through donations of money, furnishings, and rental houses, have made it possible for the Mental Health Center to set up two residential homes for the chronic mentally ill.

In our problem-sharing get-togethers we find that, although each person's situation is unique, there are many common problems, ranging from those which seem trivial (but which can be difficult to contend with), such as lack of personal care and poor grooming, sleeping and eating too much or not enough, to more serious problems, such as lack of motivation, inability to handle money (patient gives it all away or spends it all on street drugs), refusal to take medication, bizarre behavior, delusional thinking, paranoia, occasional violence, and suicide attempts. Another common problem for family members is the feeling of being tied down and not able to live one's own life. Families of a chronic mentally ill person find it difficult to travel or to maintain much of a social life.

Our own social life has become practically nonexistent, not necessarily because our friends have deserted us due to the stigma of mental illness, but because of the unpredictability of our son's illness, and because, after coping with the many problems it causes, we have little energy left over for entertaining.

The financial burden of mental illness is another big problem which families must face. When insurance (if there is any) runs out as it eventually does in most cases, not even well-to-do families can handle the frequent hospitalizations at exorbitant rates (about $200 a day in Boulder), and the many psychiatric sessions at $50 or $60 an hour. Many of the members of our group used private psychiatrists and hospitals in the beginning years of their family member's illness. As the years went on with no real improvement in their family member's condition, these families turned to the Boulder County Mental Health Center for help.

When all the above problems are considered, it can be seen that deinstitutionalization has in some ways made life for the families of the chronic mentally ill more difficult than it was for my mother-in-law back in the days when lifelong hospitalization was the fate of most of the mentally ill. But most of us, I'm sure, would rather that our schizophrenic relatives had a chance to be rehabilitated in their own communities than to be interned for a lifetime in a mental institution. We need, however, all the help we can get in coping with these problems, and the mental health professionals do not always cooperate with us. In fact, they often ignore or oppose us. Two incidents which happened to our family illustrate this uncooperative attitude: Our son was at one time under the care of a private psychiatrist in California who, after treating him for many months, decided that the best medication for him was lithium and fluphenazine. He was doing well on this medication, but suddenly decided to leave California and come home to Boulder. For 6 months he refused to have therapy or take any medication, and during all that time he was in remission. We began to think a miracle had happened, but suddenly, for reasons we do not know, he began to decompensate and was soon in very bad shape. We tried to persuade the doctors to give him the medication he had been doing well on 6 months previously, but they would not listen. It was not until he had spent long periods in three hospitals (private and state), and had mutilated his tongue and lips, that he was finally given lithium and fluphenazine, and gradually improved. The second upsetting incident occurred when I called our son at a halfway house where he had been living, and was told that he had been sent to the psychiatric hospital because he had jumped in front of a car. When I called the hospital, the staff member on duty denied that he was there. Most members of our family group have similar stories to tell.

One mother complains that her daughter's psychiatrist refused to communicate with her and did not even tell her what he thought was wrong with her daughter. Over and over, in our problem-sharing meetings, members reveal their resentment toward the professionals who ignore them, make them feel guilty, and neither give them practical advice on handling the patient nor information about the patient's illness.

Consumer-advocacy groups like FFAMI are spreading across the country. One of their goals is to become a potent force which can command the respect and attention of mental health professionals. All of us who are concerned with the mentally ill must work together to alleviate their great suffering and do what we can to help them "bear the unbearable." I think that the greatest problem I face with our son is not knowing what to say to him when he asks, "Mom, what am I going to do with the rest of my life?"

The Author

Mary Jean Willis is founder and president of Families and Friends of the Adult Mentally Ill, Boulder, Colorado.

Voluntary Action by Relatives and Friends of Schizophrenia Sufferers in Britain

by John Pringle and Peggy Pyke-Lees

Abstract

The founding of the National Schizophrenia Fellowship (NSF) is described as a response to the failure of the professional mental health community to meet the needs of schizophrenic individuals and their families. Since its inception, the NSF has engaged in four types of activities: education, political lobbying, policy formulation, and research support. Examples of each type of activity are given, illustrating the efficacy of such consumer-oriented organizations in coping with serious mental disorders such as schizophrenia.

How and why the National Schizophrenia Fellowship came to be started in the United Kingdom and what it does are described by John Pringle, its President and Founder, and by Peggy Pyke-Lees, its General Secretary from 1974 to 1981.

John Pringle: The National Schizophrenia Fellowship grew out of one young man's schizophrenic illness and his family's experience of it. When our B. began behaving in a bizarre way, the most prestigious and venerated university where he was studying did nothing about it for a year. They neither took professional advice nor even deigned to inform us, the parents. They sacked him finally at 48 hours' notice, because he was shouting insults at tutors and refusing to come out of his rooms. So B. came back home, dazed and bewildered, to an equally bewildered family. Plainly he and we needed help, but how to get it, where to look, and, more importantly, what to look *for*? Our family doctor— marvelous doctor about anything physical and a much-loved friend—admitted knowing nothing about mental illness. Consulted frantically by letter and phone, the family circle were at sixes and sevens. Some indignantly asserted that B.—the charming and brilliant B.—could not possibly be "ill." He probably had some adolescent hang-up, they said, and would snap out of it, left to himself. Some thought he must be got away from home, sent "round the world" or to a cousin who was farming in Kenya. (Belief in the therapeutic virtues of travel and the open air lingers on.) Somebody else had heard of a first-class doctor in Vienna (or was it Zurich or L.A.?) who had done wonders for the son or daughter of that friend of theirs.

I got used to this cacophony of voices in the next few years. What family in our position hasn't? I also got used to living in a fog. I visited mental hospitals which exuded varying degrees of bleakness and pessimism, or perhaps they were only reflecting my own pessimism back to me. I interviewed psychiatrists, who told me different things but mostly tried not to tell me anything. Or so it seemed. I became a connoisseur of the emollient dismissive, "Well, we shall just have to see how we go, shan't we?" or, with a ghastly smile, "Very important for *us* to keep cheerful." In the midst of all this bluffness, my heart warmed to the man who said, "We don't seem to be doing *anything* for B., do we?"

Reprint requests and requests for further information should be sent to The General Secretary, National Schizophrenia Fellowship, 79 Victoria Road, Surbiton, Surrey, UK KT6 4NS.

It took 2 years before we got a diagnosis, though looking back it would seem to have been an open-shut case, and many more years before we could obtain treatment or care which made any kind of sense. No doubt at all times and places, systems of medical care are perceived differently by providers and "consumers." In the Crimean War the British War Office was convinced that their supply of bandages and similar comforts for the wounded met all reasonable requirements and that Florence Nightingale was fussing unnecessarily. A hundred years later a similar disjunction between official assumptions about "community care" of mental illness and the reality is accurately described by Peggy Pyke-Lees, who puts our family's situation and problem in the setting of what the "paper aims" were.

Peggy Pyke-Lees: The concept of community care envisaged in Britain by the Mental Health Act of 1959 encouraged psychiatric hospitals to discharge their patients and to empty their beds. It was clearly understood that discharged patients were going to be cared for by benevolent local authorities who would provide homes and hostels, short-term and long-term, supervised and unsupervised, as well as a range of other facilities including day centers, rehabilitation units, and social clubs. A regular income was to be available under a new system of social security to those patients whose disability prevented them from working, plus a rent allowance to those who were not living at home. Arrangements were to be made by the Department of Employment to provide retraining schemes and jobs. What in fact happened? The numbers of beds in psychiatric hospitals was drastically reduced; it became as hard to get into a hospital as, in former days, it was difficult to get out of one. Even those who were admitted had no security of tenure until they were recovered enough for an independent life in the community.

Lack of community care facilities and lack of communication between services meant all too frequently that patients were discharged suddenly from the hospital and that those who had homes to go to, went to them. Many such families were given no prior warning of the return home of their patient; many of them were confronted by daily and nightly problems they had not expected and did not know how to deal with, and in all too many cases there was no communication whatever from hospital to relatives who found themselves unexpectedly looking after a bewilderingly difficult patient. These relatives did not know that there were supposed to be services helping them, and many of their attempts to discover via the family doctor or consultant psychiatrist, or via the social worker or the clerk in the local Social Security Office, met with dismal failure.

In addition to all the other difficulties, there was the fear, shame, and stigma of having at home a relative who could not work or take part in ordinary daily life. Often, the inclination to hide the situation from neighbors and friends, and even from members of the family outside the immediate home, was stronger than the need to get support from those who should have been in a position to help. The stigma is still strong and must have been an important factor in preventing the whole situation about the care of the chronic schizophrenic in the community from being dragged into the light of day until May 1970.

John Pringle: In May 1970 I put together some of our experiences in an article which was published anonymously in *The Times*. My sole object had been a hope that publicity would stir some very apathetic hospital authorities and others into action. I wanted controversy. I did not get it. What I got was a shoal of letters from *Times* readers with more horror stories, all saying that their experiences had been carbon copies of ours. Many of my correspondents urged that a society or group ought to be formed that was specifically concerned with the problems of schizophrenia and its aftercare. At length, after difficulties of money and organization, a Fellowship was established and fortunate indeed we were to attract Mrs. Pyke-Lees to become our first General Secretary.

Peggy Pyke-Lees: The first task of the Schizophrenia Fellowship was to discover what the facts of the situation were and, to this end, a professional survey was undertaken by Professor J. K. Wing and Mrs. C. Creer into the needs of relatives of sufferers from schizophrenia. Since a continuing aim was to enable people everywhere to understand the difficulties experienced by those who had had schizophrenia and by the families and friends who were caring for them, a series of publications was started. These included extracts from letters shedding light on the experiences of families who were deeply concerned about the lack of proper accommodation and employment for their loved relatives, whose earlier expectations of independent living in the community seemed to have vanished. They also showed anxiety for other members of the family whose lives had been shattered into social isolation as they withdrew from friends and neighbors because of the stigma and fear attaching to the disease.

An 18-year-old boy was acutely ill in a mental hospital. His parents had not been told what his illness was, or how it was proposed to treat it. They had been refused an appointment with the consultant. The mother, in her distress, took a day off from work and traveled 30 miles to the hospital. She sat outside the clinic where she knew the doctor would be. After she had waited some hours, the doctor came to her and said, "I understand you have been waiting to see me. There is nothing I can tell you. Your son will never be better than he is now"—and he walked away. With advice from the National Schizophrenia Fellowship (NSF), a second consultant opinion was arranged, and it is good to report that the boy is now out of hospital and doing well.

Much of the original purpose in publishing information about schizophrenia and its effect on patients and their families was to inform the Department of Health and Social Security about the need for improvement in social provision. Professional workers joined the Fellowship in general agreement that the time had come for a reappraisal of the whole situation of provision. This was largely owing to two factors:

- Firstly, that patients quite clearly continue to be disabled, and vulnerable to relapse, even though they have spent only a brief time in the hospital—or perhaps nowadays no time at all.
- Secondly, the rediscovery that "community" (that is, nonhospital) care also has deficiencies, sometimes quite as great as those of hospitals.

Later, there were encouraging indications that the Fellowship's words were being listened to with attention since the Government White Paper published in October 1975, "Better Services for the Mentally Ill," indicated in its provisions that the Fellowship's words had indeed been heard with attention and that their recommendations had had a noteworthy impact. In addition to all the educational work, and based upon it, it had therefore become and continues to be the Fellowship's task to put pressure on statutory authorities nationally and locally so that they will improve facilities everywhere for the care of schizophrenics.

One publication is worthy of special note. A brief pamphlet simply entitled "Schizophrenia" was produced in response to members' requests. It emerged that many members only learned many years after the beginning of the disease what the diagnosis had been. No one had ever told them what it meant or what the likely outcome was. They frequently became aware of the diagnosis from reading it on a certificate or from being told by a clerk in the Employment Office or the Social Security Office. A basic statement about schizophrenia was produced which was made available to members. In fact, one of the members sent a copy of this document to the national press where it received a great deal of good publicity and has since had a steady sale, including many requests by professional workers of all kinds—family doctors, social workers, and, more recently, magistrates and the police.

That community care for chronic schizophrenics has to a large extent devolved upon the police and the prison service is not widely known. Patients who have been discharged into the community after a long hospital stay all too often find themselves in the hands of the police and sometimes in the courts. Originally incredulous that a schizophrenic was refused readmission to a hospital which had been his home for 29 or more years, Probation Officers telephone the Fellowship for help in finding somewhere for their client to live which would provide the necessary support. As the Minister of State, Home Office, said in March 1977, "It is no part of a civilized policy to put the mentally ill in prison and to make prisons the receptables of those whom no other agency in society will accept." But such is the effect of the policy of community care that, as the "Report of the Work of the Prison Department 1976" pointed out:

> Mentally ill people are entering prisons and Borstals in increasing numbers and people of previous good personality, whose offenses frequently stem solely from their illness, are now being refused admission to psychiatric hospitals and are, instead, being received and detained in prison establishments.

In November 1977, Dr. J. H. Orr, the Director of Prison Medical Services, commented on the difficulties and distress of the prison service that so many psychiatric patients are finding their way to prison. He went on to say:

> . . . but it was felt that if the prison service was seen to be effectively dealing with the problem, there would be an even greater reluctance on the part of mental hospitals to accept dangerous and possibly disturbed offenders. There was no doubt that mentally ill prisoners should not be in prison, and should be transferred to hospitals; we should not take steps which might cause people outside to conclude that the mentally ill were in their proper place in prison.

Recent publications by the NSF have drawn attention to this tragic and disgraceful situation.

In "Home Sweet Nothing" (May 1979), the Fellowship has proposed the development of campus communities comprising a range of sheltered environments, where the need for continuity with minimal disruption can be met, and methods of rehabilitation and criteria of assessment can themselves be properly assessed. The desperate need for appropriate residential accommodation for mentally disturbed people was also emphasized in the 1976 Annual Report of the Salvation Army:

> An unfair burden has been placed on such organizations as the Salvation Army who always have large numbers of mentally disturbed men and women sleeping in their hostels. The 1959 Mental Health Act opened the doors of mental hospitals to discharge a stream of patients, who without adequate preparation, were expected to re-enter society and cope with the demands of daily living. . . . The vast majority became rootless wanderers, unemployable, frequently charged with criminal offenses. Today there are more than seventy thousand people who have been in a mental hospital for a period of two years or more and who have been discharged without adequate provision. . . . The Salvation Army does not complain. . . . But it does feel most strongly that this great area of social necessity should be examined in depth by the statutory authorities.

The NSF, having attracted much support from professional workers and other national voluntary organizations, plans to bring the campus community concept into existence as a national experiment.

An important part in all this educational process is increasingly being played by people who have had schizophrenia themselves and, often with symptoms controlled by medication, are back at work and ready to speak about their experiences. Such contributions are listened to with great attention, and some of the Fellowship's members of this kind are becoming more articulate about the sort of help which has been of value to them and any other kind of support which they would have found useful at different stages in their illness.

While all this educational work was going on, the Fellowship had attracted a considerable correspondence not only from people all over the country, but also from all over the world, many of whom were surprised to hear that there were others in situations similar to themselves. Every item of publicity, whether on the radio or television or in newspapers or weekly journals, produced hundreds of letters, many of them describing the writer's own traumatic experiences and nearly all of them asking for help. Every week therefore, during these early years in the life of the organization, brought increasing demands for help to the Fellowship's office—the quest for information and advice has grown enormously. Among those seeking help are professional workers in all disciplines, some of whose inquiries are of a practical nature, e.g., housing, or disability benefits, while others are concerned with ways in which it may be possible to help families by bringing them together in NSF groups in those localities where such groups do not already exist. It is, of course, largely because of its members' own experience that the Fellowship is able to give practical help and make suggestions which, it is now clear, are of value to those trying to find out, sometimes desperately, what should be done to help their relatives and themselves.

Increasingly also, NSF voluntary coordinators (the name given to those people who put members in touch with each other locally) are being looked to for advice and practical help by all kinds of people, not only other NSF members, in their home district. Residential study weekends for voluntary coordinators are being arranged so that plenty of time can be given to exploring the sort of guidance that would be helpful to different kinds of inquirers, and to encourage voluntary coordinators to have a greater belief in their own ability to help each other—in fact, to help them acquire greater self-confidence in what they are doing. This experimental weekend study, with its followup "refresher day" after 3 months, promises well and the Fellowship is grateful to the Mental Health Foundation for funding this experimental project.

The number of local NSF groups has grown, as well as the amount of activity carried out by their members. By July 1979, the number of voluntary coordinators had increased to 135. There is a wide range of local activities from regular befriending of each others' relatives, to the planning and carrying out of adult education programs, to the organization of local concerts and galas. All these events, carried out in the name of the Fellowship, bring rewarding new contacts in the neighborhoods where they happen, as well as eliciting greater understanding by neighbors and friends. Members in one London Borough arranged among themselves an emergency telephone service, an example which is now being followed in other areas; while another NSF group organized weekly country walks and other outings in which they are joined by their patients from the hospital. A growing number of Fellowship members are invited as speakers to groups of social workers, health visitors, general practitioners, and Community Health Councils as well as to various local voluntary organizations. Some members have had the distinction of addressing meetings of the Royal College of Psychiatrists.

Another type of work now being carried out by the Fellowship is the planning and undertaking of national research projects. The appointment of a fulltime Research Officer led to a detailed examination of the best way to provide long-term accommodation, together with the availability of occupation or employment. As a result of this study the Fellowship hopes to enable the provision of some kind of residential facilities to help in this most difficult of all fields on an experimental and flexible basis (cf. campus community concept mentioned above). Another pioneering task has been carried out by a full-time adviser/coordinator who worked for two years to oil the wheels of communication between the different kinds of professional workers and families in need. The resulting report, "Tied Together With String," gives an account of 2 years' active study of the care available for schizophrenics and for their relatives. The author's words reflect "confusion, not only in relatives but in many professional workers also." It is made clear that the isolated suffering, despair, and anxiety of many relatives and patients are not simply the result of psychiatric illness or of living with someone who is ill.

> The traumatic experience of accepting a diagnosis of schizophrenia is similar to bereavement or loss in the demands it makes on an individual to make painful adjustments to what may seem bearable.

Those who are responsible for providing health and social services are finding this report of great interest so that it is being read and its implications studied.

> Relatives who sincerely feel that a patient is not getting the right treatment . . . often dare not take action for fear of recrimination damaging future prospects. Their fear is often legitimate.

The National Schizophrenia Fellowship, which is a registered charity, is run by a Council of Management composed of 12 elected members and four honorary officers. Finances are always a difficulty. Members are gradually discovering ways of raising funds, and support has been given by some helpful and generous Trusts. In addition the Fellowship receives a substantial grant from the Department of Health and Social Security.

In any article about the work of the National Schizophrenia Fellowship, it should be mentioned that news of its existence has spread widely to other countries who have read in professional journals of its various publications. Two have been translated into German and are about to be translated into Dutch. There are now national Schizophrenia Organizations in New Zealand and in Australia, both brought into being by members of the NSF. The Fellowship is closely in touch with members in other countries who are trying to stimulate a Schizophrenia Fellowship into being in their own part of the world.

The word "research" is always an emotive one when the great disabling diseases are being considered. Research into the cause or causes of this or that disease is a steady fund-raising motif and not less in this field than in all others. But while the Fellowship takes no part in controversies which rage from time to time about the nature of schizophrenia and the treatment or lack of treatment that should be meted out to it, members have been particularly helpful with the research into the cause of schizophrenia which is being undertaken by the MRC Neurochemical Pharmacological unit in Cambridge. There a study is being made continuously of post-mortem brain tissue from people who have had schizophrenia in their lifetimes. There has been thoughtful cooperation from relatives in letting research workers know of any sudden sad event in their family so that arrangements could be made for post-mortem brain tissue to be conveyed immediately to the laboratory. The provisional results of this attempt to identify physical factors in the causation of schizophrenia are of promise and interest.

It is impossible to escape the conclusion that during these last few years there has been a change in attitudes as far as schizophrenia is concerned, and that that change owes a lot to the work of the National Schizophrenia Fellowship in Britain. The fact that so much now is spoken, broadcast, televised, and written about schizophrenia—however inaccurately at times—is creating an interest and awareness that here is a major disabling condition about which society needs to be concerned. Increasingly—but still painfully slowly—people are coming to understand that it is one of the great disabling diseases of the world. With this greater understanding, there will be a more sensitive awareness of problems that arise so that with any luck there will be a preparedness in society to find solutions to the problems caused by this tragic disease.

The Authors

John Pringle is President and Founder and Peggy Pyke-Lees was General Secretary from 1974 to 1981 of the National Schizophrenia Fellowship, Surbiton, Surrey, United Kingdom.

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How Families Evaluate Mental Health Professionals, Resources, and Effects of Illness

by Deborah F. Holden and Richard R. J. Lewine

Abstract

Evaluations by families (of chronically mentally ill individuals) of mental health professionals and resources were solicited through a mail survey. The respondents, largely better educated, white, and female, indicated a generally high level of dissatisfaction. Emotional support, information, and aftercare resources were identified as particular areas of concern. The survey findings present a challenge to mental health professionals to reconsider the effects of chronic mental illness on the family and the needs of the non-ill family members.

The families of schizophrenic individuals comprise a group of persons requiring professional attention for two reasons: First, these families represent a vital resource in the treatment and rehabilitation of the schizophrenic individual (Lamb and Oliphant 1978; Hatfield 1979). Between one-half and two-thirds of psychiatric patients return to their families after discharge, thus placing a substantial burden on the family for the ex-patient's readjustment (Lamb and Goertzel 1977; Minkoff 1977). Second, the families of the mentally ill have needs in their own right, aside from their role in the care of ill family members. As pointed out by Hatfield (1978), it is at the risk of their own well-being that the family undertakes the care of a chronically disturbed member.

Traditionally, professional attention to the families of the mentally ill has focused on the family's role in the development and maintenance of deviant behavior (Laing and Esterson 1964; Lidz, Fleck, and Cornelison 1965). There has been far less concern with the impact of the schizophrenic person on the family after the onset of illness (Kreisman and Joy 1974). There is ample evidence that the adjustments required to deal with deviant behavior and to care for the schizophrenic individual combine to create a severe and chronic level of frustration and tension in the family (Creer and Wing 1974; National Schizophrenia Fellowship 1974; Hatfield 1978; Parents of the Adult Mentally Ill 1979). Nevertheless, there continues to be a general lack of professional awareness of and response to the families' needs, as evidenced in part by the growth of self-help groups for families and friends of the chronically mentally ill (Lamb and Oliphant 1978; see family articles, this issue). Such self-help groups often form when group members' needs are not met through more traditional channels (Hatfield, in press). More direct evidence of families' dissatisfaction with services has been presented by Hatfield (1978) in a survey of the Schizophrenia Association of Greater Washington, a voluntary self-help organization of former patients and relatives of patients. Although the respondents in Hatfield's survey reported a high level of contact with professionals, they indicated a low level of satisfaction with professional services. Nearly half reported that the services had no value for them. Families and friends provided more effective support than did the professionals.

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The survey reported here was undertaken to assess a larger sample of family members than previously has been done and to identify in greater quantitative and qualitative detail the families' dissatisfaction with professional services and the areas of their greatest need.

Methods

Copies of the survey[1] were sent to the presidents of seven family groups representing five geographical areas: Community Mental Health Organization, Inc. (Englewood, NJ), Friends and Family of the Chronically Mentally Disabled (Denver, CO), Friends and Family of the Adult Mentally Ill (Boulder, CO), Support, Inc. (Lakewood, CO), Alliance for the Mentally Ill, Dane County (Madison, WI), Parents of Adult Schizophrenics (San Mateo, CA), and Families Unite for Mental Health Rights, Inc. (Oreland, PA). The organization presidents were asked to distribute the surveys among their members.

In a covering letter accompanying each survey, potential respondents were asked to evaluate their contact with mental health professionals. As reflected in the questions, the survey was intended to assess satisfaction with level of involvement with mental health professionals and the services received, as well as to identify areas of need. The majority of questions were in a forced-choice format, with respondents instructed to choose the one response that best characterized their situation. Since some people failed to answer all the questions and those data for which there was more than one response were eliminated from tabulation, the sample size varies from question to question. A number of open-ended questions invited elaboration of problems or concerns surveyed, while a final question asked respondents to comment about areas not covered in the survey.

Results of this survey were sent to those families providing return addresses. Anonymity of the data was ensured by removing any identifying information from the surveys, and no record was kept to link any individual's name with a survey.

A total of 500 surveys was mailed to the various groups; 203 (41 percent) were returned, a typical response rate for surveys of this type. Of the 203 returned surveys, 169 individuals (83 percent) took advantage of the request for ad lib comments. We make use of both the quantitative and qualitative data in summarizing the results.

Results

Characteristics of Respondents and Ill Family Member (see table 1). As members of the self-help groups surveyed are not a representative sample of relatives of schizophrenic individuals, interpretation of the survey findings must be made in light of the select nature of the sample. Survey respondents were a relatively advantaged group in education and occupation. Respondents were predominantly female, typically mothers of the ill individual. Their group membership indicates a high level of concern for the ill family member as well as their willingness to seek help and support from others when troubled.

Seventy-one percent of the ill family members ($n = 198$) were men. Fifty-six percent were between the ages of 25 and 34. Thirty-three percent of the ill family members ($n = 194$) were living at home at the time of the survey; 40 percent were in some type of outpatient group-living arrangement or apartment; and 27 percent were inpatients. The majority of ill relatives had received a diagnosis of schizophrenia (71 percent; $n = 145$); the remaining 29 percent had multiple diagnoses, diagnoses unknown to family members, or diagnosis of a chronic mental illness other than schizophrenia.

Satisfaction With Involvement in Treatment

Families' descriptions. Family members reported dissatisfaction both with the nature and level of their involvement in treatment. Many families reported that their involvement with professionals left them feeling guilty and defensive.

> To proceed on the assumption that the illness is caused by malparenting is very damaging because these attitudes are transmitted by innuendo if not directly. This results in increased guilt felt by the parents and decreased ability to accept the diagnosis and impairment.

More typically, families were confused, felt left out of treatment, and felt ignored by professionals. The exclusion from treatment planning eroded the family members' confidence in the individuals making the decisions.

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[1] Copies of the survey are available from the second author.

Table 1. Characteristics of family members responding to survey

Characteristic	Number	Percent
Age		
< 25	1	—
25–35	13	7
35–44	12	6
45–54	60	31
55–64	78	40
65–74	29	15
> 74	1	—
Sex		
Male	50	26
Female	146	74
Race		
White	194	99
Black	1	—
Asian	1	—
Marital Status		
Single	6	3
Married	156	80
Divorced	18	9
Widowed	16	8
Education		
7–11 years	9	5
High school	49	26
Some college	39	21
College graduate	93	48
Employment		
Professional/business	40	24
Semiprofessional/lesser white collar	78	46
Skilled/semiskilled laborer	15	9
Homemaker	37	21
Relationship		
Mother	137	71
Father	32	16
Spouse	6	3
Sibling	17	9
Child	1	—

> Each doctor seemed to make a different decision, and I was never helped to understand why. I'm not sure what to think. I was left in the dark. Everything was frightening because unexplained.

Quantitative survey results. A majority of family members (54 percent, $n=183$) felt that mental health professionals had not involved them in the treatment of their ill member. Sixty-six percent of family members ($n=196$) reported dissatisfaction with the frequency of contact with professionals, 98 percent of these dissatisfied family members preferring increased contact. Sixty-seven percent of the respondents ($n=183$) reported that they lacked confidence in individuals making decisions about treatment.

Family members reported that contacts with professionals left them feeling frustrated and powerless (table 2). Despite their frustration, the majority of families (53 percent, $n=158$) continues to see mental health professionals as the most appropriate source of help when problems arise with the ill family member (table 3).

Satisfaction With Help Received

Families' descriptions. Family members reported dissatisfaction with the help they had received in dealing with the family member's illness. A primary source of dissatisfaction was the failure of professionals to provide families with basic information about the illness and its management. This failure to provide relevant information extended from the time of diagnosis through the period of the patient's re-entry into the community.

Many families reported that professionals were vague and evasive in talking with them about the ill-

Table 2. Family member's primary response after working with mental health professionals

Response	Number	Percent
Confidence	13	8
Guilt	4	3
Powerlessness	21	13
Frustration	60	38
Anger	6	4
Understanding of schizophrenia	5	3
Learning of coping strategies	15	9
Contacts with professionals not helpful	34	33
Total	158	100

Table 3. Primary resource to families in times of crisis

Response	Number	Percent
Police	25	16
Neighbor	1	—
Family member	27	17
Friend	8	5
Religious advisor	3	2
Mental health professional	83	53
Family doctor	11	7
Total	158	100

ness. Some complained that professionals' efforts to avoid labeling only confused them. When the illness was given a name, they were better able to move toward acceptance and understanding of what they would face with the ill member. Typically, what information and understanding families had acquired about the illness was achieved slowly, inefficiently, and through much personal effort.

Another major source of dissatisfaction was what families perceived to be a lack of professional support during the period of the patient's resocialization into the community. Although families reported a lack of professional support throughout the course of the illness, this lack was most acutely felt when the patient returned to the community. During this period, many families experienced a feeling of abandonment by professionals and a sense of frustration at the lack of practical information and coping strategies they had acquired in the period of contact with professionals.

> We have so many questions! Could we be more helpful to our son? Should we "push him out" to sink or swim or be protective? What has the doctor learned about the patient that could help us help him?

Families reported that professionals were least helpful in directing them toward community resources. Families were frustrated by difficulties they encountered in finding suitable living arrangements and employment for the ill member.

> The rooming houses and halfway houses are not fit for animals. Whenever my son leaves the hospital, we have to start searching for a place for him to live. Most of the time we can only find him a room in an undesirable neighborhood which is overpriced. He is forced to have all meals in restaurants, which he cannot afford. He keeps himself clean only if the necessities are provided for him. There is no supervision and, before long, since he cannot function properly, he lands on the street or in the gutter because he is evicted from his room. He leaves his clothes wherever he happens to be.

Many families felt that independent living situations failed because of the lack of outreach support or supervision. Many also expressed particular concern about the lack of followup monitoring of medication.

Families reported that they were given little help or advice about coping with bizarre and disturbing behaviors. The lack of information about what might be realistically expected from the ill member compounded their difficulties.

> I need practical ways of dealing with day to day difficult behaviors.

> I would like consultations about what I could realistically expect of my son.

Periods of crisis are particularly stressful, as resources are generally inadequate. Many family members reported their frustration at having to involve the police in order to obtain help.

> There is no help available until after an aggressive act has occurred.
>
> The only way that I can currently get my wife help is by attesting to and swearing out a warrant for her arrest.

Quantitative survey results. The majority of family members (74 percent, $n=190$) reported dissatisfaction with the help received from professionals in dealing with the family member's illness (see table 4). Consistent with the qualitative descriptions, the quantitative results indicate a lack of basic information about the illness and its management as a major source of dissatisfaction.

Sixty-eight percent of the survey respondents ($n=170$) were given information about diagnosis within 2 years of the family member's first breakdown. Thirty-two percent were either given information about diagnosis between 2 and 11 years after the initial breakdown or were not given any information about the official hospital diagnosis. Seventy-five percent ($n=186$) were told of the diagnosis by a mental health professional, 15 percent by a nonpsychiatric medical professional, and 10 percent by a nonprofessional. Of those told by nonprofessionals, most were told by other family members. The majority (77 percent, $n=195$) felt that at the time they learned of the diagnosis, its meaning was not adequately explained, typically because it was too vague (see table 5). The relationship between source of information and the adequacy of explanation is presented in table 6.

Apparently, information about the use of medications was insufficient. Medications were used in management of the illness with 95 percent of the ill individuals ($n=199$). Fifty-three percent were given information about why medication was being used. Only 24 percent were informed about the possibility and nature of side effects which might result from the use of medication. Sixty-six percent of the respondents ($n=186$) were dissatisfied with the use of medication with their family members. Sixty-one percent of the re-

Table 4. Family member's satisfaction with mental health professionals

Degree of satisfaction	Number	Percent
Very satisfied	4	2
Generally satisfied	46	24
Generally dissatisfied	61	32
Very dissatisfied	79	42
Total	190	100

Table 5. Reasons for inadequacy of explanation of diagnosis

Reason	Number	Percent
Too vague	51	35
Too technical	6	4
Not thorough enough	45	31
Completely avoided	35	24
Other	9	6
Total	146	100

Table 6. Relationship between source of information and the adequacy of explanation

	Adequacy of explanation	
	Adequate	Inadequate
Source of Diagnosis	*n* (%)	*n* (%)
Mental health professional	34 (25)	101 (75)
Nonpsychiatric medical professional	8 (29)	20 (71)
Nonprofessional	2 (11)	17 (89)
Total	44	138

spondents who indicated dissatisfaction with the use of medication ($n=118$) reported that their greatest concern was that medication was not checked properly. Thirty-two percent of those dissatisfied felt that there was too much medication, 9 percent felt that there was too little medication, and 4 percent felt that medication was changed too frequently.

Fifty-nine percent of the respondents ($n=191$) reported that in periods of crisis, resources were inadequate.

Effects of Schizophrenia on the Family

Families' descriptions. By the families' reports, the effects of schizophrenia on family life are profound.

> No family member was untouched in this dramatic change in our lifestyle.
>
> Living with schizophrenia is like tiptoeing through a minefield. You know what you may expect, but not when, and the continuous tension is terrific.
>
> The feeling of helplessness is, I feel, the hardest to bear.

Family relationships are severely stressed as a result of illness-related tension.

> This ordeal for her was another ordeal for all of us. Where there sometimes was complete concern for her well-being and her recovery by some members of the family, there was the anger and hostility from other family members.
>
> His brother and sister at times have been torn between compassion and hostility toward him because of his erratic behavior.

Families frequently reported concern for the neglect of personal needs as well as the needs of other children in the family. Leisure time and social contacts were often restricted, energies depleted. Families had difficulty adjusting to disturbances in routine. For example, unusual sleeping and eating habits of the schizophrenic member disorganized the daily habits and schedules of other family members.

Health problems were seen as stress related. The most frequently mentioned were depression, insomnia, hypertension, heart attack, and alcoholism. Finally, many families described financial hardships which resulted from the illness.

Quantitative survey results. Seventy-seven percent of the families ($n=187$) reported increased family tensions since the occurrence of schizophrenia in the family. Eighteen percent of the families reported increased support and closeness, and 5 percent reported no change. Of those families experiencing increased family tension, 25 percent reported a major family disruption such as divorce which they perceived to be related to the stress of the illness. Forty-seven percent of these families reported health problems which they felt to be a result of increased tension in the family.

Those behaviors of the ill member which presented the greatest difficulties for family life are presented in table 7.

The financial costs of the illness presented serious problems for 32 percent of the respondents ($n=196$). Forty-two percent of the families experienced moderate financial strain, with a total of 74 percent being financially affected. The cost of the illness itself (e.g., treatment, medication) was the main reason for increased financial burden for 52 percent of those experiencing financial difficulty ($n=144$). For 39 percent of those experiencing financial strain, the failure of the ill member to provide for himself or herself presented the greatest difficulty.

Discussion

As pointed out by Lebow (1982), survey data of this sort are liable to many problems of reliability, validity, and sampling biases. Clearly, the respondents in this survey

Table 7. Ill family member's behavior presenting the most difficulty for the family

Behavior	Number	Percent
Aggression	36	24
Withdrawal	14	9
Social inappropriateness	20	13
Unpredictability	25	16
Irrational beliefs	37	24
Talking to self	4	3
Poor hygiene	10	7
Not contributing to household tasks	2	1
Other	5	3
Total	153	100

are not representative of all family members of schizophrenics: they are predominantly the mothers of ill relatives, white, better educated, and actively involved with mental health issues as manifested in their membership in self-help groups. We must, therefore, interpret the results of the survey with some caution.

Given the methodological caveat above, we found that family members were consistent in their presentation of problems and in their evaluation of professional services. The difficulties faced by these families caring for a schizophrenic member are numerous and professional support of families has been viewed as insufficient. This is true with respect to concrete support (such as advice, information) and emotional/attitudinal support. They expressed a desire to be recognized in their own right and to be more involved as partners in treatment planning.

Information emerged as a particular area of concern, a not surprising finding given the educational level of most of the respondents and their demonstrated ability to use information (in the formation and implementation of their self-help groups). We see the professional's responsibility as determining how much information is desired by family members and providing as much as lies within his or her area of expertise.

We might speculate that family members' expectations for professional help are unrealistically high and that no matter what the professional response, families would be dissatisfied. However, the families' comments were inconsistent with this interpretation. Generally, the respondents had a realistic picture of the illness and its prognosis. Repeatedly, families reported a need for realistic and practical guidance. They were seeking information and support, not simply looking for reassurance or easy answers. Although families reported being frustrated by their contacts with professionals, they continued to look to professionals for help and desired a closer working relationship with them.

These findings present a challenge to professionals to reevaluate the level and nature of their contacts with some families of schizophrenic individuals. Attitudinal and behavioral changes on the part of professionals may be necessary to the establishment of a working relationship with family members. The formation of such an alliance is the first step toward both easing the family's burden and increasing their effectiveness as caretakers. We cannot tell, from this survey, how general the findings are. Nevertheless, it appears that there exists a substantial group of family members for whom a major shift in professional attitude would be most beneficial.

If professionals are to work effectively with families of schizophrenic persons, further delineation of the families' needs is required. The findings reported here reflect the dissatisfactions and problems of a group whose personal, financial, and social resources are above average. The respondents' group affiliations suggest that they are active help-seekers, and we might expect that they have been articulate and persistent in their search for resources. Even with such a high level of personal resources, professional services have come up short. Thus, we may infer that the needs of those not represented in this survey are even greater than suggested by these findings. We do not know, for example, how lower class and minority groups are coping with the sorts of burdens imposed by schizophrenia. Indeed, we do not even know if the burdens are similar. Additionally, the largest group of respondents are parents. The problems faced by siblings, spouses, or children of schizophrenic individuals might be quite different from those faced by parents. Family concerns might also vary according to stage of the illness or certain other factors such as age or sex of the ill member. In short, we are only beginning to appreciate the problems faced by families and require more information if we are to be of help. Further description of the problems faced by families of the chronically mentally disabled and a different model for professional response to these problems are needed.

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Supportive Family Counseling

by *Kayla F. Bernheim*

Abstract

Traditional family therapy has been based on theories of families as etiological agents of schizophrenia. Such a view impedes cooperative relationships between professionals and families of schizophrenic individuals. An alternative approach, supportive family counseling, is described. Its goal is to provide information, emotional support, and recognition that family members have their own needs. The difficulties facing professionals who want to engage in this form of family intervention are discussed.

Care of the chronically ill schizophrenic patient has changed markedly in the past two decades. Pharmacological treatment can decrease the severity and disruptiveness of symptoms for many patients. Further, the sociopolitical emphasis on deinstitutionalization has created the expectation that even those with moderately impairing symptoms will live the large part of their lives in the community. In short, current thinking emphasizes medication and community mental health. As a result, ever increasing numbers of chronic schizophrenics, in varying degrees of remission, are being returned to or maintained in a community setting.

However, it is generally acknowledged that community support systems such as halfway houses, sheltered work environments, and structured recreational activities are in woefully inadequate supply. Further, many patients are apathetic about or actively resistant to participating in such programs, while some simply cannot function in those settings. Thus, families of schizophrenic patients bear an increasing burden for the chronic care of their ill relatives.

Clearly, leaving the hospital is far from the end of the rehabilitation process. While some patients recover much of their cognitive and social functioning, many others continue to suffer from chronic disruption of thinking, feeling, and relating. Among the residual symptoms which the schizophrenic patient may display are deficits in thinking, affective responding, activity level, and social skills (Creer and Wing 1975). In addition to problems created by the patient's behavior, families must cope with periods of worsening symptoms and possible rehospitalization, monitoring medication, finding community resources for their impaired relative, a constriction of their social lives, and emotional and familial conflict about the resolution of various issues connected with the patient's illness.

While the ability of the family to provide an emotionally benign, predictable environment may be a key factor in the ability of the patient to remain in the community (Brown and Rutter 1966; Rutter and Brown 1966; Brown, Birley, and Wing 1972; Leff 1976; Vaughn and Leff 1976; Wing 1977), the presence of a mentally ill member has profoundly disruptive effects on family life and severely strains the family's capacity to provide a rehabilitative environment. Thus, any plan for long-term placement of a schizophrenic person which involves living with (or an ongoing relationship with) other family

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members should include provisions for helping the family understand and cope with the problems that can be expected to arise. However, this aspect of placement is rarely given the consideration it deserves.

The purpose of this article is to describe a particular kind of contact with families who have a schizophrenic member in which the goal is to help families develop maximally adaptive expectations and behaviors with respect to the various tasks they face. The label "supportive family counseling" seems appropriate for this sort of work since it implies that the family is basically healthy (or at least that its adaptive capacities rather than its pathologies will be the focus of attention), and that the goal is to offer support and information in the face of real environmental stresses.

Supportive Family Counseling: Differences From Other Approaches

Supportive family counseling is different in purpose and structure from various other kinds of contact with families who have a schizophrenic member.

Family Therapy. Supportive family contact should not be confused with family therapy as the philosophies, goals, and strategies are very different. The family therapy model is based on the assumption that disturbances in the family system have caused the illness (Lidz 1958; Wynne et al. 1958; Bowen 1960; Haley 1969; Bateson 1972; Erickson and Hogan 1972; Foley 1974). According to this view, schizophrenia only *appears* to reside within the patient (called the "identified patient"); it is actually an illness of the family as a system. Thus, the goal is to cure the schizophrenia by reorganizing the basic family structure.

Supportive family counseling involves minimal etiological assumptions (although most of its proponents believe that schizophrenia has a significant biological component). The only assumption is that schizophrenia is a chronic condition such that most patients will remain somewhat impaired and, therefore, dependent upon others to fulfill at least some of their needs. The patient is not expected to achieve a normal level of independence. The eventual aim of family therapy, to get the family to "let go" of (i.e., extrude) the patient, stands in contrast to the goal of supportive contact: namely, to foster the family's willingness and ability to maintain long-term involvement as caretakers, even if the patient does not live at home. On the assumption that caring for a chronically ill family member is physically and emotionally stressful, and that chronic stress decreases one's ability to cope effectively, the goal is not to cure the illness, but to relieve as much of the stress as is possible and to increase the patient's and the family's ability to live with the illness successfully.

Differences in strategies follow from these philosophical differences. The family therapist manipulates the family structure by making process comments; the content of the family's concerns is often considered unimportant (if not pathological). The supportive professional assumes a much more didactic role. He or she gives information and makes specific suggestions about the family's present concerns.

The family therapist and the family often have widely disparate agendas. Family members want to know what is wrong with the patient, what causes the patient's bizarre behavior, what can be done about it, and what they can do to help. They hope for a medical explanation and direct advice about practical matters. What they get instead is the idea, rarely expressed directly, that there is nothing really wrong with the patient, that the patient's odd behaviors are the family's fault, and that they should change the way they relate to each other.

Aside from being a remarkably threatening idea, such a notion is also counter-intuitive to families. Prepared by the medical model, they find it difficult to imagine that the locus of the disorder lies outside of their relative who is behaving so bizarrely. If he is not malingering, then surely he must be ill! Further, since the therapist's agenda is expressed only indirectly, the family may feel confused, distrustful, and disappointed without quite knowing why. In fact, none of their immediate needs are being met. Unable to express their frustration directly to the therapist, such families are at risk for increased anger toward the patient as well as for dropping out of therapy, often taking the patient with them.

Information Gathering. Under the assumption that schizophrenia is rooted in a disturbance of early parent-child relating, some therapists choose to conduct sessions that are designed to elucidate these early relationships. It is presumed that understanding the etiology of the illness will aid the therapist in treating the patient. Family members are encouraged to focus on the past with particular emphasis on ambivalent feelings, and on questionable parental decisions or behaviors. Sometimes the patient's accusations against the family are used as the starting point for the exploratory process.

The clinician tends to behave passively, asking leading questions and responding to questions or concerns nondirectively. Often the family responds to this lack of direction by enlarging their recollection of errors. Not only do they feel at fault, but they also feel as if the damage has already been done and they are powerless to change the situation. The consequent depression may rob the family of motivation and energy with which to deal with present realities.

Avoidance. Clinicians who see the goal of therapy as separation of the patient from the family may be reluctant to enter into any kind of relationship with the family. Particularly if they see themselves as allies of their patients in the struggle against the smothering family, they may perceive contact with the family as collaboration with the enemy, and therefore treasonous. Instead of directly communicating their position to the family, they will neglect to return phone calls, rely on the patient to communicate all treatment decisions, and respond to familial questions and concerns as if they were inappropriate intrusions into the professional arena. Often such behavior is thought to help the patient to act more independently. When information is required of the family, these clinicians will typically seek it through the social worker as intermediary.

Developing a Therapeutic Alliance

Whether the family's role in the development of schizophrenia is substantial or nonexistent, concrete or nonspecific, interventions which ignore the family's needs have the same predictable outcome: They increase the family's level of anxiety, guilt, depression, anger, and frustration, and they lower the level of adaptive responding of those people on whom the patient may most need to rely. Instead of alienating the family through avoidance, passive-aggressiveness, or guilt-induction, supportive family counseling tries to develop a therapeutic alliance with family members who can be helped to provide maximal support to the recovering patient. The goals include not only securing the family's cooperation, but repairing their self-esteem and relieving feelings of helplessness which may be seriously reducing their energy stores.

Communicating Acceptance

Initially, what is communicated is the professional's deeply held belief that the family is doing (and, indeed, has always done) the best it can with its available resources. The turmoil and disruption the family has experienced is acknowledged and members' attempts to take care of themselves and each other are respected. While families often behave in disturbed and disturbing ways, many of these behaviors can be seen as responses to the schizophrenic member's behavior and are, in any case, attempts to cope with that behavior despite significant pain and confusion.

Further, much of what appears pathological in the family's initial presentation may result from various expectations they have about the meetings. Family members, particularly if they have had previous contact with mental health professionals, may expect to be accused of having caused the illness, of being mentally ill themselves, or of having mismanaged the patient. As a result they are likely to be guarded, angry, and resistant.

On the other hand, family members sometimes appear to want to be told "where we went wrong." Whether out of unresolved guilt feelings or the expectation that the therapist has that objective, or out of difficulty in facing present realities, these people appear depressed and find it difficult to make any decisions.

The family may expect to be given simple answers to difficult questions about etiology, prognosis, and other aspects of the illness. They may appear frustrated and annoyed when such answers are not forthcoming. They may imply that the therapist is incompetent or withholding information, and may sometimes remove the patient from the treatment setting. While much information can and should be given, the family will have to learn about and accept the limits of our knowledge and the relative unpredictability of the disorder.

Often, the family understands the purpose of the sessions to be solely to help the patient. They expect little sympathy for the practical problems they face and even less for the emotional turmoil they experience. These families appear passive and unspontaneous, offering information in response to questions but revealing little of themselves.

Finally, families may expect to be coerced into painful situations. For example, they may expect the professional to tell them to keep the patient at home (or not to) when they would strongly prefer the opposite.

Sometimes all of the members of a family share the same expectations, but often they differ. Rarely are these expectations verbalized in a straightforward way. Rather, families who perceive the professional as an adversary, or strictly as the patient's advocate, or even as an omniscient authority protect themselves in whatever ways they can—through emotional withdrawal, superficial compliance, stubbornness, or a host of other strategies. In any case, the first order of business is to dispel erroneous expectations so that the family is prepared to work actively with the counselor. This usually can be accomplished through maintaining an unfailingly supportive posture and responding directly and actively to the family's concerns.

Stylistic Issues

The effectiveness of counseling families with a schizophrenic member depends heavily on adopting a style of working that is consistent with their needs. Remembering that the family's capacity for adaptive decisionmaking has been decreased by chronic stress, the counselor tends to be active, engaging, and structuring. He or she may offer concrete advice, suggest that family members behave in certain ways, develop homework assignments, and in other ways take more control than one does in other kinds of work. The assumption is that initially many families cannot "figure things out" on their own. They may want, and need, a time-out from decisionmaking in which to regroup their defenses. The counselor plays a parental role, if necessary, instead of allowing the family to flounder and fail to make needed decisions.

Understanding that the mental health maze poses a formidable challenge to families seeking help for an ill relative, the counselor wears multiple hats—acting as advocate or social worker for the family when necessary. He or she helps to clarify the treatment options and attempts to ensure that the family's concerns are taken seriously by the treatment team.

Realizing that the patient's presence and behaviors may be stimuli for highly charged, ambivalent feelings that impede effective coping, the counselor frequently chooses to conduct sessions without having the patient present. Interestingly, patients rarely object, nor do they show more than a mild level of curiosity about what goes on in the family sessions. Again, flexibility is the rule—it may be helpful to include the patient in some sessions but not in others. Likewise, it may be useful to see various combinations of family members at different times, instead of seeing the whole family together each time. If some family members are unwilling to participate at all, the counselor usually sees whoever is interested rather than refusing to see the family at all.

Effective work in the early phases of supportive counseling may entail a purposeful suppression of clinical judgments as the counselor focuses on adaptive aspects of the family's functioning while ignoring, at least for the moment, dysfunctional patterns. Further, the counselor consistently describes as normal and expected the various feelings of family members, paying particular attention to accepting their frustrated and hostile feelings toward the patient. The aim is to reduce immobilizing feelings of guilt, despondency, and anger through the communication of respect and concern. Once such a relationship is established, the counselor is in a position to educate family members about schizophrenia and counsel them with respect to specific areas of concern.

Educating the Family

It is astonishing how little information is generally offered to families of schizophrenics. If the patient has been given a diagnosis, family members have not been told what the diagnosis signifies or what its implications for etiology, treatment, and prognosis are. Many family members believe that schizophrenia means "split personality" and have a hard time understanding how the term applies to their ill relative. Left in the dark about the chronic nature of the illness, they often have unrealistic expectations of the patient and of treatment. Thus, they are at risk for trying any "miracle cure" that comes along and may resist standard treatment suggestions.

Families who have an understanding of the illness and its implications find it much easier to cope with schizophrenia's fluctuating course than those who do not. They are less likely to panic inappropriately if symptoms worsen slightly. Being somewhat more tolerant of deviant behavior, they are less apt to make unrealistic and stressful demands on the patient to function beyond the level of his or her competence. Further, their support of medication and other treatments tends to improve when they understand what each is meant to provide.

The supportive family counselor can play an important role in the education of family members. Specifically, he or she:

1. Labels and describes the illness. Applying a label to a mental illness can be quite helpful to the patient and the family, even if the label is as initially frightening and stigmatizing as "schizophrenia" is. Its use implies that the professionals know what is the matter and serves to decrease the bewilderment and panic the family may be experiencing.

Schizophrenia can be described as the physiologically based tendency to become confused and disorganized in characteristic ways under stress. By creating an analogy to ulcers, headaches, or other stress-responsive disorders, the counselor demystifies the illness. The distinction between schizophrenia and split personality is carefully described. This sort of description lays the groundwork for obtaining the family's cooperation in the patient's treatment. Some families seem to profit by a fairly sophisticated discussion of how the brain transmits information, how that system may have gone awry in schizophrenia, and how medications may work. (Some patients may benefit from the same discussion.) Of course, we cannot explain to families exactly what causes schizophrenia since we do not know ourselves. However, offering a general explanation which emphasizes that schizophrenia is an illness with a recognized treatment helps the family change its focus from guilty obsession about the past to problem solving oriented to the present.

2. Discusses various treatment options. Families often undercut attempts to provide treatment because they lack information. This is most often the case with respect to the need for ongoing chemotherapy. Hearing the patient's complaints about side effects, observing some sedation or muscle rigidity, being concerned about the possibilities of drug addiction, and left in the dark about the sorts of therapeutic benefits they should watch for, family members may collaborate with the patient to resist further treatment. The professionals who are working with the patient often see such collaboration by relatives as purposeful sabotage designed to keep the patient in a sick and dependent role. However, family members are usually acting in what they perceive to be the patient's interests, given the information they have available. Once attention is paid to their concerns and their questions are answered, they often become staunch supporters of the treatment regimen.

Families may also discount or minimize the value of adjunctive treatments such as occupational therapy or sheltered workshop placement. They may urge the patient to get a "real" job and "stop fooling around." However, a discussion about the skills necessary to get a job (e.g., adequate attention span, ability to follow sequential instructions) and the function of these therapies in evaluating and enhancing the patient's competencies is often enough to enlist their support.

3. Helps the family set realistic expectations. By educating the family about schizophrenia's uneven course and by discussing the residual impairments that accompany the illness, the counselor helps the family properly evaluate the patient's capabilities. The patient's history and initial response to treatment can be used to offer the family a tentative prognostic statement, designed to help them develop realistic expectations for the future. The prognosis is related as concretely as possible to the family's concerns—for example, the patient's ability to become self-supporting, to control undesirable behaviors, and to achieve social goals. In the face of the vague, wait-and-see attitude of many professionals, families may hold onto unrealistic goals for a long time, continuously upsetting themselves and the patient who never does seem to "snap out of it." Emphasizing that rehabilitation is a stepwise process allows the family to grieve for their lost dreams gradually while maintaining a realistic sense of hope that the patient may continue to improve.

4. Develops the family's monitoring skills. It is quite normal for families with a recovering schizophrenic member to watch the patient closely. The family, of course, wants to prevent the patient from getting sick again, although, paradoxically, their efforts often increase the stress the patient feels. With a clearer understanding of what to look for and

why, the family is able to narrow its focus, thereby becoming more efficient and less upset and upsetting. Often, family members learn to observe accurately signs of medication side effects, the current level of various symptoms, the sorts of situations in which the patient functions well or poorly, and the often subtle precursors to a psychotic episode. In this way they are able to collaborate usefully with the treatment team and put their emotional need for vigilance to good use.

Developing Strategies for Daily Living

In addition to educating the family about schizophrenia, its treatment, and its prognosis, the counselor helps the family to make decisions about the handling of various day-to-day problems. For example, families need to discuss how to maximize the patient's independent behaviors, whether the patient should live at home or elsewhere, what sorts of limits or controls should be set concerning bizarre or annoying behavior, whether the family should vacation out of town, under what circumstances the patient should be rehospitalized, and what sort of explanation should be given to extended family or friends of the family.

Of critical importance is the family's ability to find a comfortable middle ground between martyring one or more healthy members in the service of caring for the impaired relative and behaving callously or irresponsibly. Families seem much more likely to err in the former direction than in the latter. While it is important for most people to feel that they have done the best they can for the impaired family member, even to the point of having made substantial sacrifices, families who lack energy and investment in their healthy members find their resources quickly sapped. Such families need to be encouraged to take better care of themselves and to make use of whatever community facilities exist to relieve their burden.

Areas of Potential Conflict

Responsibility. The supportive family counselor is "on the line" in the sense of being called upon to answer direct questions—with information, solutions, and advice. This is a position that mental health professionals rarely find comfortable. Indeed, few are willing to assume so much direct responsibility for the comfort and well-being of the client. Most prefer to take a "hands off" approach in which the therapist may help a client learn how to make good decisions but never make a decision or even suggest a course of action for a client.

Further, while demystifying schizophrenia often lowers the anxiety of the family, it can raise the anxiety of the professional who will have to admit to the family that he or she has neither a magical cure nor infallible suggestions. In working to reduce the discrepancies in theoretical and practical knowledge between mental health professional and family member, the counselor reduces his or her own "expert" status in the bargain. It is difficult enough to make decisions that affect other people without exceedingly good guidelines to go by; it is harder still to do so while shedding the mantle of omnipotence that gives credence to educated guesses. However, what is lost in placebo effect is usually gained in a shared sense of cooperation and affection.

Dependency. Like the chronic schizophrenic patient, the family may rely on the counselor more heavily than feels comfortable. Particularly if the patient has been ill and untreated for a few years, if the family is disorganized and dysfunctional for other reasons, or if previous professionals have been aloof or disparaging, the family may thrust the counselor into a parental role, requesting advice on the most minute details of living and making few independent decisions. Further, they may profit by maintaining contact with the counselor for years after some suitable coping patterns have been established, although such contact can be brief and infrequent.

Chronicity. Many therapists find it frustrating and draining to work with schizophrenic patients; the same issues of chronicity and the necessity for lowered expectations face the family's counselor. Just as the patient's symptoms may flare up after a period of relative quiescence, the family may experience periods of resurrected grief, or renewed overinvolvement. And just as the patient loses motivation and becomes chronic over the course of the illness, so does the family get worn down by the weight of its burden as the years go by. The counselor must be prepared to cover the same ground many times, often with no long-term resolution possible, and to experience feelings of impotence with respect to long-term prognosis.

Conflicting Loyalties. While it is frequently the case that what is good for the family is also good for the patient, it sometimes happens that functional family members must choose between themselves and the patient. Should the disruptive patient be present at the family Christmas party, given that family members will feel ashamed and on edge if the patient comes? Will the patient feel left out and hurt at being excluded? Should a parent accept a lower paid or less interesting job because the hours are better suited to transporting the patient to therapeutic activities? Should the patient live at home when this living arrangement massively constricts the lives of others but the only alternative is an unstimulating boarding home? Faced with these and other questions, families always agonize and often develop torturous solutions in an attempt to compromise or to find a way to finesse the decision. It is sometimes necessary for the counselor to take a stand, to suggest that the family ought to satisfy the needs of its healthy members in certain instances, or at the very least to help the family feel as little guilt as possible when they do make such a decision. This task can be particularly difficult when the family's counselor is also the patient's therapist, but bucking the tide by advocating for the family within the treatment team is never easy.

Overcoming Old Biases. For most of us, our academic and clinical training has left us ill-prepared to take on the role described above. We are prepared to view the family as being responsible for the patient's problem. We are prepared to view independence from one's family of origin as the right and proper goal of treatment. We are prepared to divulge to the patient or to the family little of what we know—and of what we do not know. Overcoming the biases of our training (and perhaps of our own lingering adolescence) can be difficult. The families with whom we work can help us make the transition if we acknowledge their enormous desire and potential for supporting the patient's rehabilitation.

Summary

As is true for our work with schizophrenic patients, our goals for their families must be modest. These people are faced with uncertainty, responsibility, conflict, sacrifice, and stigma, often over a long period of time. Helping them learn to weather crises and to resign themselves to unfulfilled expectations is sometimes the most for which we can hope. However, one mother pinpointed the value of reaching even this goal by saying, "I can accept his getting worse, occasional hospitalizations, anything that comes along, if only I know there's somebody to talk to who understands."

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Developing an Enforceable "Right to Treatment" Theory for the Chronically Mentally Disabled in the Community

by Betty L. Nordwind

Abstract

Historical developments, mental health approaches, and applicable legal authorities are examined in arguing a legal basis for pursuing greater treatment benefits for chronically mentally disabled persons in the community. Mental health lawyers have traditionally been concerned with patients' right to treatment while in the hospital. Lawyers are called on to examine the plight of (and to extend advocacy for) the chronically mentally disabled in the community.

The purpose of this article is to review certain historical developments, various mental health approaches, and applicable legal authorities to see if there are sound legal bases for pursuing greater treatment benefits for chronically mentally disabled persons living in the community.

Definitions and Preexisting Assumptions

The Chronically Mentally Disabled. As used here, this terminology refers to young, middle-aged, and elderly persons who have severe or persistent mental or emotional disorders that seriously limit their functional capacities relative to the primary aspects of daily living such as personal relationships and interactions, living arrangements, and employment opportunities. This definition is based upon, and should be read in conjunction with, the extensive definition developed by the National Institute of Mental Health (1976, 1977).[1] It should be further noted that as described herein, "chronically mentally disabled persons" includes many individuals in addition to those released from state mental facilities during the 1960s, and specifically includes those individuals *currently* being turned into chronically disabled persons by a variety of existing forces.[2]

Treatment. In the context of this article, treatment refers to the full panoply of benefits, services, and rights which comprise the necessary elements in the lives of many chronically disabled persons. Thus, "treatment" includes housing alternatives, employment, and vocational training opportunities, adequate financial assistance and social work services, educational programs, and health and mental health care options. "Treatment" is presumed to be tailored to the needs of each individual and to be far more extensive and complex than simply the more traditional and limited definition of "mental health care and treatment."

Community. "Community," in the sense discussed in this article, refers to anything outside the four walls of a state mental institution, and specifically includes nursing and boarding homes, and other

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[1] As used in this article, the definition of chronically disabled individuals *includes elderly persons.*

[2] While members of the former group (released from state hospitals in the 1960s) are referred to as "deinstitutionalized" persons, members of the latter group (becoming chronically impaired by virtue of present factors in the 1970s) are usually considered to be part of the "revolving door" syndrome.

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"ghettos" where many seriously disabled clients live and/or frequent.

Preexisting Assumptions. This article is based upon this writer's observations, conversations, discussions, and readings over the past 4½ years, fueled by a strong desire to understand how the public mental health system actually does and theoretically should function, on behalf of chronically mentally disabled persons. It is specifically based upon the writer's experiences in metropolitan Denver, Colorado (Denver, Adams, Jefferson, Boulder, and Arapahoe Counties), although there is little to refute the belief that the situation in Denver is anything but indicative of state and local mental health systems operating throughout the United States (Bassak and Gerson 1978; Koenig 1978; Deinstitutionalization, *Public Employee,* 1979). Having "lived" with a remarkably poor, although well-reputed and expensive, public mental health/social service care system, this writer is both frustrated and angry and hopes by this article to stir other advocates to positive corrective action to compel affirmative changes in treatment of the chronically mentally disabled.

Historical Developments

The great "deinstitutionalization" movement of the 1960s, about which much has been written, described, analyzed, and critiqued (General Accounting Office 1977; Bassak and Gerson 1978; Koenig 1978; Deinstitutionalization, *Public Employee* 1979; President's Commission on Mental Health 1978), was spawned by three sets of factors: (1) the discovery and use of psychotropic medications such as chlorpromazine (permitting for the first time significant alleviation of psychiatric symptoms without resort to physical restraints), (2) legislative authorization (federal and state) for the development of community mental health centers (CHMHCs) (ostensibly creating an extended community care system for the mentally ill), and (3) the advent of Medicaid, Title XIX of the Social Security Act (providing for federal financing of long-term care in nursing homes located in the various *states* operated by *private entrepreneurs*).[3] The result of the confluence of these three sets of factors was to set into motion the release of thousands of persons with serious mental illness who had previously been hospitalized on an extended long-term basis in state mental institutions.

With the benefit of hindsight and experience, this movement can in general be said to have been a tragic failure. Again the factors causing the failure are several, but revolve around these central points: (1) massive lack of preparedness on the part of institutional community agencies and caregivers, most particularly the CMHCs and county welfare departments; (2) professional biases toward and dislikes of the seriously disabled, multi-needy person, in favor of the less difficult, more-likely-to-succeed-in-response-to-treatment individual; and (3) the very real and substantial impairments of many of the individuals released, requiring significant long-term, innovative interventions by the institutional community caregivers (Glasscote et al. 1969; *Hospital & Community Psychiatry* 1979; Talbott 1979). The combined effect of these variables has been to turn the "back wards" of the state mental hospitals into the "back wards" of the community—into nursing and boarding homes, with many variations on the central theme (Special Committee on Aging 1976). These facilities are generally inadequate, and are poorly equipped and staffed to treat the mentally ill.

The facilities have gone unregulated by state and federal authorities for the "mental health care and treatment" offered; disclaimers of any official or formal relationship to institutional caregivers have been made by the caregivers themselves, denying the very real and significant place such facilities serve within the public mental health system.[4] There are no other housing alternatives for chronically disabled persons, and viable, coordinated community services and programs have not been developed and funded. Due to this system, the chronically disabled population has not fared well but rather has remained "institutionalized" in these "community" facilities, continuing to be as dependent and nonproductive as they were in the state hospitals 10 years ago.

What has happened is that the existence of nursing home facilities paid for by the federal government through its Medicaid program has removed the pressure on state and local governments to create any significant housing alternatives (residential spectrum of facilities); simply put, because there has always been a place for the chronic ex-patients to go, the need for other, more appropriate residential facilities (discussed below) has never been critical or clearly apparent. For similar reasons, and because of the extremely passive, dependent, nonarticulate nature of most of the chronically disabled, the community service system has remained undeveloped, uncoordinated, fragmented, and unresponsive to their many needs. Institutional caregivers, particularly the CMHCs and welfare departments, have ignored these individuals except where individual crises have demanded their attention, and have instead continued to deliver their services along traditional lines of service delivery, with little outreach and aftercare built into their programs.

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[3] See Chu and Trotter (1974). The original CMHC legislation can be found in PL 88-164, 77 Stat. 882 (1963); Medicaid legislation, Title XIX of the Social Security Act, is found in 42 U.S.C. 1396 *et seq.*

[4] Such has been the case, for example, with the Colorado Division of Mental Health & Department of Institutions.

The silent vacuum of residential, social, and vocational services and programs for seriously mentally disabled individuals has left unchanged the older generation of chronic patients, while at the same time creating a new breed of individuals who can be identified by their numerous short-term hospitalizations and stays in nursing and boarding homes—what some have called the "revolving door" syndrome or "transinstitutionalization" (*Hospital & Community Psychiatry* 1979; Talbott 1979). Thus, public mental health and social service systems may be condemned not only for what they *have not done* for the previous generation of chronic patients, but for what *they continue to fail to do* for others now coming into the system. Because of their statutory responsibilities to serve these individuals, the CMHCs must be cited with primary responsibility for this failure, with other institutional caregivers such as the welfare and health departments running a close second.[5]

Mental Health Approaches

There is a substantial and steadily growing body of literature which has analyzed and described appropriate community "treatment" program requirements for chronically mentally ill persons.[6] Basically, the recommendations for essential components for a successful community care system include the following: (1) *case management services*—a level or cadre of specially trained, typically paraprofessional persons, whose roles are to help seriously mentally disabled individuals obtain and maintain needed services, to assist such persons in alleviating and preventing the various repetitive disruptions and crises in their lives, and to help teach disabled individuals sufficient daily living and life coping skills (e.g., shopping, budgeting), so that they may achieve some degree of personal satisfaction in their lives. It has been suggested that case management staff be composed of former employees of state mental hospitals, who have a great degree of familiarity and understanding of severely disabled clients; (2) *a coordinated delivery system*—a full service, comprehensive delivery system (e.g., mental health, health, vocational, educational, income maintenance, recreational aspects) "appropriately linked," so that chronically disabled individuals can, with relative ease, obtain needed services rather than being subject to varying and inconsistent agency policies and practices. In large cities such as Denver, this coordination has not occurred; services are fragmented and suffer from interagency isolation. Clients and even service personnel are forced to deal with different agencies on a piecemeal basis, causing unnecessary and often unsuccessful expenditures of time, energy and financial resources; (3) *a spectrum of residential facilities*—a range of graded and regulated community facilities (public, private, and not-for-profit), such as independent living apartments, shared dwellings, cooperative living arrangements, personal care or family care homes, group homes, lodges and small boarding homes, designed to permit easy movement in and out according to the client's needs for structure, supervision, and support change. The philosophy underlying creation of a system of residential programs is that most chronically disabled individuals function best in small, homelike environments where independence is encouraged and developed, and where care *more excessive than* actually needed (e.g., cooking, cleaning, laundering) is not provided (Test 1976). One of the more recent developments has been the increased utilization of U.S. Department of Housing and Urban Development (HUD) low-income housing programs, particularly the HUD rent supplement program, to create additional "normalized" settings in the community for seriously disabled clients (Bradley, Allard, and Liegey 1978).

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[5] For a fuller understanding of the original CMHC legislation and its amendments including those passed in 1975, see Glasscote et al. (1969), Chu and Trotter (1974), and Foley (1975). The CMHC legislation is found in PL 88-164, 1963, and PL 94-63, 42 U.S.C. 2689 *et seq.*, 1975.

[6] See, for example, the entire issues of *Hospital & Community Psychiatry*, March 1976 and January 1978; Kincheloe and Hagar (1974); Lamb et al. (1976); Tertiary Aid and Prevention Team (1976); and Test and Stein (1977).

Other principles for implementation of an adequate community care system are that major support from institutional caregivers must be provided to third parties who live with, or have very close contact with, disabled clients. The literature does indicate that substantial and readily available intervention (i.e., 24 hours per day, 7 days per week) on the part of caregivers to third parties such as boarding home managers and close family and friends helps to quell disturbances and prevent further conflict. It has also been found to encourage third parties to continue attempting to work with disabled clients, since it reassures them that outside assistance will be provided if needed. Adequate community care for chronically disabled persons also requires a reversal of the traditional mental health approach to treatment. Community care requires that formal caregiving agencies such as CMHCs actively recruit, solicit, and follow seriously disabled clients. The term "aggressive" outreach has been used to describe the approach. Traditional mental health care has it that mental health providers should wait for the client to appear and seek service, since only when the client "wants to change" will treatment be effective. While there are many debatable issues, not the least of which is protection of personal privacy, the evidence is fairly clear that dynamic outreach programs help clients reduce the problems in their lives, and that normal mental health delivery programs are ineffective in stopping dysfunctional conduct (e.g., rehospitalization because of the exhibition of "crazy" behaviors) (Test and Stein 1977; James and Abbott 1978). The initial conclusions of those few caregivers who have developed successful community programs for chronically disabled individuals are that while the programs do not dispense with such requirements as maintenance dosages of psychotropic medications, the mental health service systems would do better to concentrate most of their resources (personnel and financial) on teaching clients daily survival skills, instead of relying on the more familiar "insight-oriented" therapy sessions. Further, these programs suggest that reliance upon medically oriented definitions of mental illness such as "schizophrenia" and "manic-depressive" disease is not helpful to problem solving for the chronically disabled individual and that it is more productive to focus on the individual's skill levels, dependency needs, and dysfunctional behaviors which actually cause so many of the individual's problems.

Existing large-scale, successful community care systems for the chronically disabled are woefully few, and it would be safe to say that no state, regional, or local government has held itself out as having satisfactorily developed an adequate and comprehensive care system for chronically mentally disabled persons. There are a few such programs led by several individuals who have achieved some success and have received national attention: Paul Polak, formerly of Southwest Denver CMHC; Leonard Stein and Mary Ann Test of Madison, Wisconsin; John Beard of Fountain House in New York City; Rhett Potter of Ogden, Utah; and Hillary Sandall in St. Louis, Missouri, among the few. The National Institute of Mental Health has recently begun a small pilot program of grants to encourage development of community support systems.[7] Official rhetoric and policy statements now support such approaches (Asher 1977; Brown 1977; American Psychiatric Association 1978), but the reality is that the basic systemic problems remain untouched, the clinicians remain uninterested in and frustrated by the clients, and the individuals themselves go on playing out their fruitless lives.

Legal Theories

Case Law. In the early 1960s Morton Birnbaum, a lawyer-doctor, wrote that the necessary return (or legally, the "consideration") for an individual involuntarily confined for mental illness ought to be adequate and appropriate treatment offered by the mental health professionals. Since that time, the "right to treatment" theory has developed and been enlarged upon by numerous courts led by Chief Judge David Bazelon of the U.S. Court of Appeals for the District of Columbia (Birnbaum 1960; Bazelon 1974, 1975*a*, 1975*b*).[8] The first cases were brought by individuals confined to psychiatric hospitals seeking individual relief. The first decisions held that there was a statutory and possibly a constitutional right to treatment, when an individual was involuntarily confined for mental health treatment. The decisions found that treatment must be provided in the environment *least restrictive* in nature so that minimal interference with the individual's right to liberty occurred (Developments in the Law 1974; National Association of Attorneys General 1976). Thereafter systemic attacks were brought against governmental bodies on behalf of large numbers of individuals, seeking massive changes in treatment programs and requesting development of programs in less restrictive settings.[9] The next logical step occurred in 1975 when a U.S. District Court in Washington, D.C., held that in accordance with the laws of the District of Columbia, treatment in less restrictive settings was a statutory right and the nonexistence of such alternatives in the community effectively voided that right. Therefore, the Court ordered creation of less restrictive alternatives, although implementation as late as *1979* has been terribly slow in coming. The most recent step that has occurred has been the filing of several class action suits on behalf of mentally ill persons confined to state hospitals, requesting relief in the form of creation of less restrictive community alternatives with a full spectrum of services and programs, with standards to regulate quality of care, and evaluation and enforcement mechanisms.[10] At least one of these suits has been settled successfully by the plaintiffs and has apparently precipitated the creation of a system of community care alternatives for the institutionalized persons.[11]

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[7] See, in particular, NIMH Request for Proposal (RFP) No. NIMH-MH-77-0088 and No. 77-0081 concerning community support system (CSS) projects. This RFP was issued in July 1977 and several projects, including one in Colorado, have been funded. For further information concerning the NIMH efforts, contact Judith Turner, Division of Mental Health Services Programs, Community Support Project, NIMH, Rockville, MD.

Other cases have held that while in state custody for mental health care and treatment, the individual has a right to expect freedom from further harm or deterioration,[12] and that the individual has a right to minimally adequate habilitation, which includes treatment in the least restrictive setting.[13] Besides these cases, some courts have found relief for mentally disabled individuals based on a variety of different constitutional grounds, including the First, Fifth, Eighth and Fourteenth Amendments to the U.S. Constitution, and similar portions of applicable state constitutions.[14]

The cases, though legally very significant and perhaps providing relief to thousands of persons, have serious problems attached to them when viewed from the perspective of enforceable rights for the chronically mentally disabled population. First of all, no suit has yet been filed which challenges *existing* community care systems or nonsystems. The most analogous have been those recent cases requiring creation of appropriate community programs with standards, and implementation of monitoring mechanisms. These cases may either avoid entirely the problem of inadequate and inappropriate community systems by doing it "right" the first time, or they may in 5 to 10 years be faced with the same problems as now exist in Denver, Los Angeles, and New York City. In addition, no case has actually held that a specific right to treatment or type of treatment is necessary for a specific group of individuals, and courts have been reluctant to become involved in the particularities of treatment decisions made by public agencies for fear of interfering with administrative agency discretion. Review by the courts has traditionally been limited to a determination of whether minimally adequate treatment exists, and whether it is reasonable and not an arbitrary or capricious exercise of governmental power.[15] To challenge an existing community system, the advocate must be prepared therefore to argue that no system actually exists or that though it exists, it is so poor that it effectively denies treatment in the least restrictive alternative.

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[8] *Rouse v. Cameron*, 373 F.2d 451 (D.C. Cir. 1966).

[9] *Wyatt v. Stickney*, 325 F. Supp. 781 (M.D. Ala. 1971), *enforced* 334 F. Supp. 1341 (M.D. Ala. 1971) and 344 F. Supp. 373, 344 F. Supp. 387 (M.D. Ala. 1972), *aff'd sub nom, Wyatt v. Aderholt*, 503 F.2d 1305 (5th Cir. 1974); *Welsch v. Likens*, 373 F. Supp. 487 (D. Minn. 1974), *aff'd in part & remanded in part*, 550 F.2d 1122 (8th Cir. 1977).

[10] *Dixon v. Weinberger*, 405 F. Supp. 974 (D.D.C. 1975); *Brewster v. Dukakis* (E.D. Mass. 1978), final consent decree reported in 3 *Mental Disability Law Reporter* (MDLR) 44 (Jan.-Feb. 1979); *Doe v. Yuen*, No. 77-0059 (D. Hawaii, filed Feb. 23, 1977); *Caswell v. Califano*, No. 77-0488 (W.D. Mo., filed June 30, 1977).

[11] *Brewster v. Dukakis* (E.D. Mass. 1978), *supra* footnote no. 10.

[12] *New York State Association for Retarded Children v. Carey*, 393 F. Supp. 715 (E.D. N.Y. 1975).

[13] *Halderman v. Pennhurst State School & Hospital*, 446 F. Supp. 1295 (E.D. Pa. 1977).

[14] See Coleman and Gilbert (1979); note particularly Section IV dealing with litigation beginning on p. 82.

Other problems faced by advocates seeking greater relief for the chronically disabled based upon existing case law is the distinction that has been made in the past between those individuals involuntarily held and those labeled as "voluntary." The theory is that the former persons, by virtue of the compulsory state intervention, have a right to treatment, while the others do not. While several cases in the developmental disabilities area have dispensed with this distinction because it is an illusory one, different in name rather than fact, nonetheless such arguments may pose a bar to legal action to enforce the rights of many chronically disabled persons. These individuals have become "institutionalized," are totally dependent upon public agencies, and are factually helpless without them; yet they are, technically speaking, "voluntarily" receiving services.[16]

Still other difficulties which may be envisioned in any proposed major litigation effort on behalf of the chronically disabled are the high costs of those efforts, the extended commitments of time required of legal and support staff, the great dependency upon experts in winning or losing the case, and the sheer effort involved in keeping track of, and in contact with, the clients themselves.[17]

Statutes. There are several federal statutes which may be relied upon to base and/or to strengthen legal claims for adequate and appropriate community services for the severely disabled. Chief among these is Public Law 94-63, which is a compilation of several important mental health statutes passed by Congress in 1975 after lengthy hearings beginning in 1973.[18] Title I of Public Law 94-63 places requirements on state mental health agencies receiving federal mental health funds to eliminate inappropriate placements in institutional settings, to ensure creation of appropriate noninstitutional alternatives, and to supervise the community mental health centers to ensure their adherence to statutory requirements found in Title III of the Act. Title III requires CMHCs to provide "followup services" and "transitional-halfway house service" to persons discharged from mental health facilities. While further Congressional and administrative actions have not clarified the meaning of these phrases, and some confusion still remains as to precisely how broad the range of services was intended to be, the legislative history of Titles I and III of Public Law 94-63 clearly indicates a strong concern and effort to eliminate some of the injustices occurring to the deinstitutionalized population and a desire to begin providing appropriate and necessary services.[19]

Other relevant federal legislation includes the Rehabilitation Act of 1973 and amendments (prohibiting federal recipients from discriminating on the basis of handicap, which may include the failure to provide *equal opportunity* to subclasses of physically or mentally disabled persons. It also includes provisions concerning vocational rehabilitation programs for the severely disabled); Titles XIX and XX of the Social Security Act (permitting federal expenditures for a range of medical assistance, home health, social service, and housing benefits for seriously disabled individuals). It should also be noted that Title XIX permits Medicaid payments to be made to nursing homes for care of the injured and disabled, including the mentally disabled, although it bars Medicaid payments to nursing home facilities where more than 50 percent of the residents have a primary psychiatric diagnosis and are between the ages of 21 and 32 to 65). It is also worth considering the health planning laws, which at present are intended to regulate the further growth and development of health/mental health care facilities including nursing homes, although such laws do little to require affirmative changes in *existing* health/mental health care institutions and delivery systems.[20] The Older Americans Act may also provide a basis for relief for elderly mentally disabled clients.[21]

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[15] For a general discussion and analysis of the scope of judicial review over administrative agency decisions, see Davis (1972), particularly chapters 28 and 29. The thoughts of Chief Judge David Bazelon (1969, 1975*a*, 1975*b*) on the role of the courts in the mental health field are insightful and recommended reading.

[16] *Halderman v. Pennhurst State School & Hospital*, 446 F. Supp. 1295 (E.D. Pa. 1977); *New York State Association for Retarded Children v. Carey*, 393 F. Supp. 715 (E.D. N.Y. 1975). In both of these cases the courts held that the distinction between voluntary and involuntary was meaningless in the face of overwhelming dependencies of the plaintiffs on the defendants, their lack of viable options, and generally their inability to go anywhere or to do anything without assistance from the defendants. Although the plaintiffs in both these cases were mentally retarded rather than mentally ill, they provide some precedent for making a similar argument on behalf of the chronically mentally ill.

[17] There is increasing concern with the enormous amounts of time and resources which are involved in litigating a major least restrictive alternative or community care suit, and for enforcing judicial orders. A conference recently conducted by the attorneys from the Mental Health Law Project and the Public Interest Law Center of Philadelphia (PILCOP) in Golden, Colorado, apparently stressed the difficulties inherent in bringing a major suit. See, also, Ewing (1979).

[18] PL 94-63, 42 U.S.C. 2689 *et seq.* For some of the legislative history, see Health Subcommittee of the Committee on Labor and Public Welfare, 1973; Subcommittee on Public Health and Environment, 1973, 1974; *Conference Report No. 93-1524 on Health Services and Health Revenue Sharing*, 1974; Nordwind 1979).

[19] *Ibid.*

There are a variety of state laws applicable in individual jurisdictions which incorporate specific laws concerning right to treatment in the least restrictive alternative, and otherwise afford mentally ill individuals procedural and substantive rights, which can be used to bolster an argument for the chronically disabled. State laws also regulate CMHCs and specifically delineate the responsibilities of state mental health agency authorities which may have some bearing on treatment rights of the severely disabled.[22]

The mere existence of a law which seems to be intended to benefit a group of persons (e.g., the CMHC Act for the chronically disabled), does not in and of itself mean that a court will so apply the law. The courts have held that a statute must clearly state that private individuals have a right to claim its protections and/or benefits in order to be permitted to sue to enforce their rights. If a statute fails to state such right on its face, legal action on behalf of private individuals is permitted if the court can *imply* a private right of action from a reading of the statute and its legislative history, *Cort v. Ash*, 422 U.S. 66 (1975). Thus chronically disabled persons seeking relief under any of the statutes referred to above—for example, the CMHC Act or the Rehabilitation Act—will initially have to convince a court that they have a right to sue under those laws.

In sum, state laws, regulations, guidelines, and plans pertaining in any manner to mental health services should be carefully studied and analyzed in order to gain maximum advantage for severely disabled clients.

Conclusion

Community mental health centers and other institutional community agencies, both state and local, have failed to create adequate and appropriate residential, vocational, and social service programs for chronically disabled persons. These failures, which are in terms of numbers, types, and quality of programs, affect both those "older" chronic patients released in the 1960s from state hospitals and those currently in the making, by repeated hospitalizations, stays in nursing and boarding homes, and other factors. These individuals are denied realistic opportunities to pursue normal lives in "normalized" settings in local communities, and have instead become or are in the process becoming dependent, nonproductive persons, frequently exhibiting self-destructive or self-defeating behaviors. Clinical theories and practical solutions have been developed which provide a solid foundation for substantially revising current programs in relatively short periods of time—were the desire and the impetus present among CMHCs and other community caregivers. Significant progress is *not* occurring, and lip service and rhetoric substitute for fundamental changes in our mental health and social service systems.

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[20] PL 95-602 (1978) 29 U.S.C. 701 *et seq.* as amended (The Rehabilitation Act of 1973); PL 89-97 as amended by PL 93-233 (1973), 42 U.S.C. 1396 *et seq.* (Title XIX, of the Social Security Act, "Medicaid" statute); PL 93-647, 42 U.S.C. 1397 *et seq.* (1975) (Title XX of the Social Security Act).

[21] National Health Planning & Resources Development Act of 1974, PL 93-641, as amended by PL 95-83, 42 U.S.C. 300K *et seq.* See the excellent discussion and analysis about use of health planning laws in the deinstitutionalization process by Margaret Ewing (1979).

[22] See, for example, Colorado laws providing a statutory right to treatment in the least restrictive alternative, C.R.S. §27-10-101 *et seq.* (1973 as amended); Colorado laws regulating CMHCs, C.R.S. §27-1-201 *et seq.* and setting forth specific responsibilities for the Executive Directors of the Department of Institutions and the Division of Mental Health, C.R.S. §27-1-101 *et seq.*

It is now and has been for some period an appropriate time for mental health advocates to act at the behest of, or on behalf of, chronically disabled persons, and to secure for them decent housing, vocational, and social service benefits. Unfortunately, as unresponsive as the CMHCs and welfare departments have been, "mental health lawyers" have been, with notable exceptions, even *less* cognizant of or interested in treatment rights for the chronically disabled living in the community.[23] While mental health advocates have done an excellent job in securing many important procedural rights for involuntarily confined individuals, have vigorously fought for adequate treatment for institutionalized persons, and have argued strenuously in favor of proper community placement for many inappropriately confined individuals, there has been no litigation challenging on a broadly scaled basis community services and programs for the severely disabled. In essence the large body of historical, sociological, and clinical mental health data which has accumulated and documents the failures in great detail and which also proposes corrective alternatives, appears not to have been assimilated by mental health law advocates, or if it has, the advocates seem unable to know what to do about it. It is sadly ironic that the problem that several leading mental health professionals have called America's most serious mental health problem has been ignored by dedicated mental health advocates. It is conceivable that the problems are so widespread and insidious that their existence becomes taken for granted and accepted, or perhaps advocates are better prepared to identify and seek relief concerning clear-cut legal problems such as restraints and overmedication, and have more difficulty focusing on many-sided, "fuzzy" social issues that require interdisciplinary collaboration for successful resolution. Whatever the reason, mental health lawyers are significantly behind the few innovative mental health professionals who have recognized the problems and who have tried to design and implement alternative approaches. Mental health advocates need to catch up quickly, and specifically they need to review and digest some of the literature, and evaluate their own communities (statewide or local) to determine the extent and nature of the problems. There are many nuances and variations on the themes which have been elaborated in this article, and situations far better and far worse than those mentioned herein. Mental health advocates must therefore devise strategies through litigation, negotiation, or other means, which compel creation or remediation of community care services and programs for chronically mentally disabled persons in their communities.

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[23] There are, as stated, notable exceptions to the seeming lack of interest in this subject on the part of mental health lawyers. Those exceptions include Leslie Scallet and Margaret Ewing of the Mental Health Law Project in Washington, D.C., and Cynthia Barnett (1978), who wrote an article entitled "Treatment Rights of Mentally Ill Nursing Home Residents." The Barnett article focused almost exclusively on the plight of elderly mentally ill residents in nursing homes and did not elaborate on other types of chronically disabled persons in nursing homes, nor was its purpose to develop a theory for community placement. It did however chide the "mental health bar" for ignoring a "serious problem that has not received significant legal attention" (p. 692). Recently, the Legal Services Corporation Research Institute published a handbook dealing with issues of least restrictive alternatives (Coleman and Gilbert 1979). In that publication the authors note the absence of any such litigation: ". . . new models of litigation must be fashioned if remedies are to be found for those mental patients already released and suffering from the inadequacies of the aftercare system" (Coleman and Gilbert 1979, pp. 159–160). Several years ago the New Jersey Division of Mental Health Advocacy filed an *amicus* brief in a case called *Patients et al. v. Camden County Board of Chosen Freeholders et al.*, Docket No. L-33417-74 P.W. (Superior Ct. NJ Camden County), available from National Clearinghouse for Legal Services, 500 North Michigan Ave., Chicago, Illinois 60611, #19,311D. In their brief the NJDMHA present a wealth of material supporting their argument in favor of a right to aftercare. One of the articles relied upon in their brief, Saphire (1976), "The Civilly Committed Public Mental Patient and the Right to Aftercare," is an important contribution to a legal analysis of this problem and is recommended for further reading.

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Overview and Reflections

by Richard R. J. Lewine

Abstract

What seems to be a general dissatisfaction with the mental health system is discussed in the context of the inevitable problems created by chronic mental illness. Patients, families, and professionals can, instead of blaming each other for such problems, acknowledge the common difficulties and begin to seek new strategies. Each of us has unique strengths to share, but to do so requires moving beyond traditional roles.

A strong current of dissatisfaction with the mental health system and professionals runs through the articles in this issue, as well as through many of those not included. It would be too simplistic, however, to assume that everything would be solved "if only"—if only mental health professionals were more sympathetic to families, if only diagnostic labels were not used, and if only there were more jobs available. There is inherent in our work with the seriously mentally ill a great deal of frustration and anger which often is displaced onto others. Thus, for example, a therapist may take out his sense of ineffectiveness in treating schizophrenia by blaming the schizophrenics' parents for having failed in their roles (Bleuler 1978). Similarly, we must expect that anyone involved in the lives of the chronically mentally ill will face difficulties for which they will be tempted to blame someone else. Although these difficulties will not be the same for all, the sad fact about psychopathology, at least for now, is that there will be instances in which no amount of money, resources, or support will eliminate the emotional pain that it causes. This view should not be misinterpreted as a basis for giving up; indeed, it is just the opposite.

Having once acknowledged that we share a common bond in our struggle with serious mental illness and that there are no villains, we can begin to seek new strategies. In keeping with Peterson's plea that we emphasize "... what is right with us" (patients), rather than what is wrong, we can examine the previous articles for what they can teach us about one another's strengths.

We learn from Lovejoy and Peterson that alternative role models to the "bag lady" exist for chronically mentally ill individuals. Neither a formal diagnosis of chronic schizophrenia nor years in a psychiatric hospital necessarily predict an inability to live and work successfully in the community. These two former patients do remind us of the potentially detrimental effects of labeling in its undermining motivations and lowering expectations of patient and therapist alike. However, the issue of labeling is not a simple one, as implied by Bernheim's pointing to the positive aspects of providing a patient and family with a formal diagnosis. What then are we to do in the case of chronic mental illness? Do we avoid the use of diagnoses in an attempt to prevent "self-fulfilling prophecies" or do we use them to convey our understanding of what is wrong? The answer is not an easy one and will no doubt vary from situation to situation. Nevertheless, diagnoses

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do carry information and are probably best discussed as thoroughly as possible, but in a supportive, encouraging, and hopeful context. It is when we stop dealing with the person that labels can be harmful.

Another issue relevant to labeling and expectations is that of the "neo-Kraepelinian revolution." Clearly, there has been a resurgence of the importance of deterioration in functioning and chronicity of disorder in the conceptualization of schizophrenia, as reflected, for example, in the American Psychiatric Association's (1980) *DSM-III: Diagnostic and Statistical Manual*. The issue here is *not* a diagnostic one; we do not argue whether schizophrenia as defined in *DSM-III* is right or wrong. Rather, we refer to the attitudes and expectations engendered by different conceptualizations of schizophrenia. For example, one of the striking features of Bleuler's (1950) reformulation of dementia praecox as schizophrenia was his emphasis on the different courses and outcomes that occurred in the disorder. The shift from a view of schizophrenia as a disorder of progressive deterioration to one of a disorder with different outcomes allowed therapists to be more hopeful than had previously been the case. In contrast, to the extent that deterioration and chronicity are essential features in defining schizophrenia—as is now once again true in *DSM-III*—we can expect an accompanying drop in our expectations and hope for schizophrenic patients. This may well be subtle, but powerful all the same. It seems, therefore, that now is a time to guard against undue pessimism.

There has been a strong tradition in the mental health professions to view the families of schizophrenics both as causing the disorder in the ill family member and as being deviant and ineffectual themselves (Lewine, in press). However, we find in reading the selections in the Family section of this issue that families of schizophrenics can be articulate and very effective across a broad range of areas. Family members are frequently concerned about their ability to care for their ill relatives, and many have begun to look to one another for strength and help. Because we in mental health research and care have focused primarily on schizophrenics' relatives, especially parents, who are themselves schizophrenic or deviant in some way, it is helpful to be reminded that the large majority of schizophrenics' parents are not seriously ill and rear many more offspring who are not schizophrenic than who are (Bleuler 1978). Remembering this fact could contribute to the sort of attitudinal changes that many relatives of the chronically mentally ill have suggested.

Bernheim presents us with an apparent paradox: to work effectively with families, professionals must give up some of their "placebo" power by admitting that they do not always have the answers. To do so, however, raises two challenges to professionals that are implicit throughout this issue. The first challenge is to allow "consumers" (patient and family) to define, at least in part, their own needs. This is particularly difficult in the area of mental illness since the nature of the disorders with which we deal frequently interferes with an individual's perceptions and thinking. Often we must assume that we in fact "know what is best" for the patient. The second challenge is to avoid interpreting everything within a context of pathology. Because we are trained as professionals to focus on illness, deficit, and deviance, it is sometimes difficult for us to see mental health. It is frequently the case, for example, that both a patient and his family know the type and dose of medication which is most effective. However, it is difficult for mental health professionals not to interpret suggestions about medication as "manipulation" or some other evidence of psychopathology. A hidden strength to which professionals may turn is their honesty in saying, "We don't know."

There are, of course, realistic obstacles to the development of new and adequate methods for treating chronic mental illness and providing help for families: for example, economic conditions that have reduced the funds available for social services and research, laws that frequently penalize families for financially helping an ill relative, and the absence of a cure for schizophrenia. Finally, there continues to exist a pervasive social stigma associated with mental illness. Both ex-patients and the families of the seriously mentally ill have taken an important step toward eliminating this stigma by discussing their problems in public. Facing professional and public attack or scorn, they have nevertheless begun to organize and work for the improvement of our mental health system.

Unfortunately, it seems as if professionals lag behind in this area. Not too long ago, when a family self-help group was being organized, a mental health professional known by one of the family members to have a schizophrenic daughter was asked to lend his name and time to the effort. Instead, he sent a check and a note expressing concern about the reaction that such a public disclosure would cause in his department, one well known, ironically, for its efforts in community mental health. Whether the threat was real or imagined, it speaks to the long distance we have yet to travel in reaching an acceptance of mental illness. It would not seem too unreasonable to hope that some future issue of the *Schizophrenia Bulletin* would be devoted to mental health professionals who themselves have had some personal experience with mental illness; as evident in the few such discussions available, this could provide a unique and helpful perspective (e.g., Wasow 1978). As expressed by Lovejoy, "We are not only like you, we *are* you—your sons, daughters, husbands, sisters, fathers."

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Improving the Quality of Community Care for the Chronically Mentally Disabled: The Role of Case Management

by James Intagliata

Abstract

This article draws upon an extensive case management literature in order to integrate a number of key concepts and findings that must be considered by those responsible for the planning, administration, and provision of effective community care to the chronically mentally disabled. A discussion of the reasons for the current popularity of the case management concept within human services is followed by a detailed presentation of the objectives, ideology, functions, and structural elements that characterize case management systems. A series of practical problems and issues that must be addressed to effectively implement a case management system are then identified and analyzed. Finally, a set of recommendations for those developing case management systems is offered, and a number of important unanswered research questions about the delivery and impact of case management services are identified.

Although case management is not a new idea, it has gained increased popularity in the human services field in recent years, particularly as a mechanism for improving services delivery to chronically mentally disabled[1] persons. To appreciate the case management concept, it is useful to begin by examining some of the factors underlying its current popularity.

The pressing need for case management has emerged in response to two major forces that have radically changed the human services environment over the last two decades. The first of these is the rapid expansion of human service programs that took place throughout the 1960s and continued into the 1970s. As a result of this expansion, the overall availability of services increased significantly. Because public funding for these programs was provided primarily through narrow categorical channels, however, the network of services that has resulted is highly complex, fragmented, duplicative, and uncoordinated. Countless individual programs have been developed to provide extremely specialized services or to serve narrowly defined target groups. While these factors interfere with service accessibility for all potential users, the barriers are particularly burdensome for those persons whose complex problems require them to engage in multiple, disconnected programs in order to get the assistance they need.

This situation was recognized by many professionals, even during the early 1960s. For example, the President's Panel on Mental Retardation (1962) expressed concern about the ease with which consumers could secure needed services. According to this panel, the

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[1] The term "mentally disabled" is used here to refer to both the chronically mentally ill and the mentally retarded.

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concept of a "continuum of care" was a critical consideration for service system planners and involved:

> The selection, blending and use in proper sequence and relationship, the medical, educational and social services required by a retarded person to minimize his disability at every point in his life span. . . . A continuum of care permits fluidity of movement of the individual from one type of service to another while maintaining a sharp focus on his unique requirements. The ongoing process of assuring that an individual receives the services he needs when he needs them and in the amount and variety he requires is the essence of planning and coordination.

Unfortunately, the networks of services in most areas have not developed with the planning or coordination necessary to ensure quality care for consumers. For example, Test (1979) notes that most professionals' familiarity with continuity of care consists of a variety of cliches that describe its absence. It has, in fact, become commonplace to use such terms as "the fragmented system," or to refer to the patients who "fall through the cracks" or "become lost in the system."

In response to these problems increasing attention has been given to the concept of services integration, especially by federal, state and local levels of government. In the early 1970s, the Department of Health, Education, and Welfare recognized the need for improved coordination of its own programs at state and local levels, and proposed a legislative initiative, the Allied Services Act, to facilitate integration of services. The Department also began a series of demonstration projects—the Services Integration Targets of Opportunity (SITO) grants—to test various services integration techniques at the state and local levels.

Under the SITO grants numerous service integration techniques were developed and demonstrated, including client-tracking systems, information and referral mechanisms, one-stop service centers, specialized management information systems, interagency planning and service delivery agreements, computerized resource inventories, and management reorganization projects (Mittenthal 1976; Morrill 1976). The one additional feature that was common to most of the SITO projects was creation of the role of "systems agent," operationally a case manager, who was expected to coordinate system resources for individual clients and to be accountable for successful client transit of the system. Thus, the widespread use of case managers as part of SITO efforts directed increased attention to the case management concept.

A second force that has radically changed the human services system, and that has also contributed to the current popularity of case management is deinstitutionalization. Before the movement toward deinstitutionalization, many thousands of mentally disabled persons were served in large public institutions. Though the institutions themselves were frequently characterized by overcrowding and dehumanizing conditions, the institutional model nevertheless offered the potential to meet all resident needs "under one roof" and thus provide reasonable continuity of and clear accountability for care (Kirk and Therrien 1975).

When mentally disabled persons were released from institutions, however, responsibility for their care and support generally became diffused among several agencies and levels of government. The roles and responsibilities of these agencies and specific actions that needed to be taken to meet the special needs of deinstitutionalized persons were not clearly defined, understood, or accepted (Government Accounting Office 1977, p. 24). As a result, deinstitutionalized persons were forced to depend for their support on a complex, uncoordinated network of community service agencies.

Although many people could manage such a situation reasonably successfully given sufficient persistence and patience, the mentally disabled, whose own abilities to cope are significantly impaired, were generally incapacitated by it. Thus, most did not receive the services they needed, either because the services did not exist or because they were unable to obtain them on their own (Test 1979). The negative consequences of failing to provide adequate and appropriate community care to deinstitutionalized persons have received widespread attention in recent years (Lamb and Goertzel 1977; General Accounting Office 1977; Bassuk and Gerson 1978; Segal and Aviram 1978; Willer, Scheerenberger, and Intagliata 1978). In response, a number of important initiatives have been developed to address the special needs of this population.

To meet the needs of the chronically mentally ill living in the community, the National Institute of Mental Health (NIMH) has developed the conceptual framework for a comprehensive network of required services—the "community support system" (CSS)—and has provided funds to operationalize this concept through demonstration projects in 19 states and the District of Columbia (Turner 1977; Turner and TenHoor 1978; Turner and Shiffren 1979). The positive aspects of this comprehensive support approach for dealing with schizophrenic populations have been highlighted by Mosher and Keith (1980) in their review of psychosocial treatment strategies. At least 10 different potential elements of community support programs have been identified as part of the CSS concept. However, case management is considered to be the key element since it provides the mechanism for coordinating all system efforts.

There has also been considerable attention given to the need for better integration of the services provided to deinstitutionalized mentally retarded persons. In recognition of the need for better coordination of the community-based care of this population, specific services integration mechanisms were mandated by Congress in the Developmentally Disabled Assistance and Bill of Rights Acts of 1975 (DD Act, PL 94-103) and 1978 (DD Act, PL 95-602). In the 1975 version, there is a requirement that each client be assigned a "program coordinator" responsible for implementing the person's individual habilitation plan and attending to the "total spectrum of the person's needs." The 1978 version specifically mandates that coordination be achieved by the delivery of "case management services" to all eligible persons. These services are to involve an ongoing relationship between the clients and an agency or provider to ensure access to and coordination of all social, medical, educational, and other needed services.

In summary, the rapid expansion of human service programs created a sprawling, fragmented network of services. The subsequent attention given to the difficulties experienced by consumers in general, and the deinstitutionalized mentally disabled in particular, has led to the current widespread interest in services integration techniques, especially case management.

The Concept of Case Management Services

Numerous definitions of case management have appeared in the human services literature in recent years. Though they vary somewhat, their common theme suggests that case management is a process or method for ensuring that consumers are provided with whatever services they need in a coordinated, effective, and efficient manner. The specific meaning of case management, however, depends upon the system that is developed to provide it. In turn, the particular characteristics of the system are shaped by the context in which it is expected to operate. The characteristics that more fully define case management systems include objectives, ideology, functions, and structural elements.

Objectives. A variety of objectives have been associated with case management efforts. Perhaps the most fundamental of these is to enhance the *continuity of care* provided to clients. Test (1979) suggests that continuity of care, in fact, has two dimensions. The first is cross-sectional such that, at any given time, the services provided to an individual are comprehensive and coordinated. The second dimension is longitudinal, and necessitates that the system continue to provide comprehensive, integrated services over time, as well as be responsive to ongoing changes in the person's needs. This longitudinal dimension is particularly critical when case management systems are intended to serve populations whose disabilities are not only significant but also lifelong. Thus, to ensure continuity of care, case management efforts must take both of these dimensions into account.

Other objectives frequently associated with case management are the enhancement of *accessibility* and *accountability* within the service system. As mentioned previously, the current human services system comprises multiple categorical programs, each with its own eligibility criteria, regulations, policies, and procedures. As a result, clients are likely to experience significant difficulties in gaining access to many of the services they need. Case management with its provision of a designated agency or service provider to assist clients in negotiating the system is thus intended to make services more accessible. Another consequence of the fragmented character of the service system is that it becomes exceedingly difficult to assure accountability when multiple agencies are involved in meeting a client's needs. Case management is intended to enhance accountability by designating a single person or agency as responsible for the overall effect of the system (Baker and Northman 1981).

One final objective of case management is to enhance the *efficien-*

cy of service delivery within the system. In the absence of case management it is frequently reported that clients either fail to receive the services that match their needs or, if they receive services, they are provided in an improper sequence or untimely fashion. Thus, the potential positive effects of available services are greatly diminished. By fixing responsibility for developing and implementing a coordinated service plan on a single person or agency, however, case management is intended to improve the efficiency of the service system.

This objective of enhanced efficiency is sometimes equated with that of reducing costs for service delivery. While, in theory, case management might reduce costs within the system, in practice, case management often results in the identification of more client needs and the delivery of more services (Mittenthal 1976; Morrill 1976). Thus, while the specific services delivered to clients may be more cost-effective, it does not necessarily follow that total service costs per client will be reduced by case management.

Ideology. To understand the case management concept, it is also important to be aware of the ideology or belief system that accompanies it. The following components typically characterize this ideology:

- The planning and implementation of service plans must be responsive to the fact that individual clients are unique, each with their own set of strengths and needs.
- The services and supports provided to clients must vary over time in their type and intensity if they are to continue to fit the changing configuration of each client's strengths and needs.
- The level of support provided to clients should match the degree of their individual deficit. Clients should be encouraged to function as independently as they can.
- The commitment of case management services to clients must be open-ended. It is a support that must be made available around-the-clock and throughout the lifespan according to clients' needs.

If those designing a case management system wish it to operate according to these principles, care must be taken to design and scrutinize all aspects of the system so that they are taken into account (Jessing and Dean 1976). The subsequent discussion of the functions and structures of case management systems will illustrate how these aspects of case management ideology are, in fact, operationalized.

Functions. Case management is frequently presented as a process comprised of multiple functions without specifying the persons or structures responsible for carrying them out. According to Agranoff (1977), the five basic functions of a case management system include:

- Assessment of client need;
- Development of a comprehensive service plan;
- Arranging for services to be delivered;
- Monitoring and assessing the services delivered;
- Evaluation and followup.

These five functions—assessment, planning, linking, monitoring, and evaluation—in fact appear in almost every description of a case management system, regardless of its context.

There are additional functions, however, that are considered to be important components of some case management systems. While some of these functions might be subsumed under Agranoff's five basic functions, a number of them clearly expand the role to be played by a case management system. The additional functions that appear most frequently in case management systems are outreach, direct service provision, and advocacy.

The appropriate range of functions for a case management system varies with the context. Acknowledging this, Ross (1980) offers three different models for case management programs designed to serve elderly persons in need. Table 1 presents the set of functional components associated with each of the three models. According to the author, the major difference among them is the increasing amount of control over provider agencies that is exercised in the coordination model and the comprehensive model. This multimodel conceptualization is offered not to suggest that the more comprehensive models are necessarily more effective, but rather to illustrate that there is a range of options to consider when designing or implementing a case management system.

Structural Elements. While it is useful to describe case management systems in terms of goals and functions, one must ultimately discuss the specific structural char-

Table 1. Three models for case management programs[1]

Minimal model	Coordination model	Comprehensive model
Outreach	Outreach	Outreach
Client assessment	Client assessment	Client assessment
Case planning	Case planning	Case planning
Referral to service providers	Referral to service providers	Referral to service providers
	Advocacy for client	Advocacy for client
	Direct casework	Direct casework
	Developing natural support systems	Developing natural support systems
	Reassessment	Reassessment
		Advocacy for resource development
		Monitoring quality
		Public education
		Crisis intervention

[1] Ross (1980).

acteristics that are required to enable such systems to function effectively. Though the functions that define case management do not necessarily require that one create a role for a person termed "case manager," this is by far the most common structural characteristic of case management systems.

Case manager. The need for a human services generalist worker whose function is to coordinate services for the individual client has been recognized since the early 1960s (Intagliata 1978). The concept of an expeditor (case manager) was adapted by Reiff and Reissman (1965). Since that time, various labels have been used for this role including: case manager (the term to be used here), integrator, expeditor, broker, ombudsman, advocate, primary therapist, patient representative, personal program coordinator, systems agent, and continuity agent, to name but a few.

Case managers are the most critical components in the case management system. They serve as the human link between the client and the system. In collaboration with other providers, case managers ensure continuity of care to clients by ultimately determining the services, environments, providers, and duration of service that will be of greatest advantage to the consumer. In addition, the case manager has the responsibility for ensuring the achievement of the highest possible level of social, economic, and physical integration of consumers.

Specifying the particular functions performed by case managers is not a simple task. Although great care is often taken to define the scope of activities that case managers engage in, the reality is that substantial differences typically exist between officially mandated patterns of case manager activity and actual patterns of service (Caragonne 1979). The reason for this is that someone thrust into the case manager role must function essentially as a trouble-shooter, confronting and resolving a wide range of problems, many of which are unpredictable. More specifically, case managers have the unenviable task of assuring that clients receive appropriate, coordinated, and continuous care from service systems whose design provides for none of these features. As a result, persons acting as case managers must be ready to play whatever role the situation may require—outreach worker, broker, advocate, counselor, teacher, community organizer, planner, or administrator (McPheeters 1974; Turner and Shiffren 1979).

Undoubtedly, the comprehensiveness and intensity of the role that case managers assume should be tailored to fit the particular needs of the client populations being served. The case manager functions that are judged to be essential when serving one type of client may be elective or even inappropriate for another. However, three functions must be viewed as essential for case managers regardless of their clientele.

The first and perhaps most basic role that must be played by case managers in any system is *to remain aware of the comprehensive needs of their clients*. This means that case managers must be aware of, though not necessarily directly involved in, the initial intake and assessment of their clients. If these functions are assigned to other workers in the system, it is important that case managers be in close contact with them so that there is no slippage in the communication of crucial information. The assessment of client needs must be an ongoing process that does not stop after initial formal intake sessions. Thus, regardless of the role that case managers play during intake, they must stay in regular contact with their clients, remaining sensitive to and observant of changes in their clients' needs. This activity is crucial because the case manager is the only provider in the system whose responsibility is being aware of the "whole" client.

A second basic function is *to link clients to services* that will meet their needs. To do this case managers must be aware of the resources that are available to their clients. These resources include both services and entitlements (e.g., food stamps, Medicaid). To be effective linkers, it is also important that case managers function as advocates for their clients. Though individual service plans may call for referral of clients to certain services, there may be barriers that inhibit clients from actually receiving them. Potential barriers include service agencies' restrictive regulations and policies or the reluctance of many generic providers to serve clients with particular disabilities (e.g., mental illness, mental retardation). In addition, it should be noted that it is sometimes the clients themselves who resist being served or "drop out" of service. While respecting clients' individual rights to refuse treatment, case managers should actively encourage clients to help maintain their motivation for treatment. This is especially true for adults with severe and chronic mental or emotional disorders (Turner and Shiffren 1979).

The responsibility to link clients to services does not require that case managers also be responsible for making the professional clinical decisions about which services are appropriate to meet their clients' needs. If, however, the development of an individual service plan is conducted by another professional or team of professionals, it is crucial that the case manager, as well as the client, be actively involved in the process. Involvement of the case manager has several important benefits: (1) it acquaints the case manager with the rationale and expectations for the treatment prescribed, (2) it allows the case manager an opportunity to inform clinical treatment staff about the local availability and adequacy of the services being considered, and (3) it provides the case manager with an opportunity to serve as the client's advocate, raising questions about specific decisions or making alternative suggestions.

The third essential function of case managers is *to monitor the services being provided to clients.* The most basic aspect of the monitoring process is to ensure that the agreed upon services are being received. This means that case managers must have ongoing contact with both clients and their service providers to ensure that appointments are being kept. In addition, the case manager must be responsible for assessing the appropriateness and effectiveness of the services provided. To do so, the case manager must not only keep in contact with the client and service provider but, if feasible, also visit with the client while the service or program is actually being provided. This kind of firsthand contact often provides valuable feedback otherwise missed. If case managers are not given the authority to change clients' treatment plans, then there must be effective mechanisms enabling them to communicate their observations to those persons who do make these decisions.

While the three activities of assessing, linking, and monitoring are the essential elements of the case manager's role, the "process" of carrying out these activities also requires consideration. *Perhaps the most influential aspect of the case management process is the quality of the personal commitment that case managers develop toward their clients.* The case manager is the human link between the client and the system, and the only service provider concerned with and responsible for the whole client. Individual case managers thus provide a mechanism for personalizing the service delivery system. The human relationships that develop between case managers and clients should be considered a fundamental strength of the case management model, and case management programs should be structured to facilitate and capitalize on this process.

While the essential aspects of the generic case manager role have been described, case managers who are expected to meet the needs of special populations, such as the mentally disabled, must assume more intensive and comprehensive client responsibilities. The special needs of mentally disabled persons necessitate that effective case management systems provide clients with such additional supportive services as:

- Assistance with managing problems of daily living;
- Crisis intervention;
- Individual level advocacy;
- Systems level advocacy.

However, while case managers ought to have some role in providing these types of special support, the extensiveness of each of these additional case-management functions necessitates that certain aspects be delegated to other direct care staff, supervisory or administrative level staff of the agency providing case management, other specialized service agencies, and even consumer groups. A brief discussion of each of the additional supportive services will illustrate the considerations involved.

Case managers for the chronically mentally ill are commonly expected *to assist their clients with the management of simple life activities and practical daily problems.* In New York State, for example, case managers of CSS clients often provide their clients with the assistance or encouragement they need for the proper maintenance of their personal hygiene or individual households. Other supporting activities might include helping clients prepare a grocery list, accompanying them on a shopping trip, or transporting clients to a needed service if no other arrangements can be made.

Although case managers can be expected to provide some of the support that clients may need in managing daily activities, they clearly cannot meet all of their clients' direct service needs in this area. If system developers are not sensitive to this issue, there is the risk that case managers who are hired for the purpose of coordinating and monitoring the efforts of multiple direct service providers will themselves become another group of specialized direct care staff. Thus, systems planners might assign the responsibility of teaching clients community living skills to direct care staff who have special expertise in doing so. For clients who need continuous and intensive support in negotiating the community, other types of special service providers can be used.

Weinman and Kleiner (1978), for example, employed lay persons to act as enablers for chronic mental patients living in the community. These persons spent several hours each day with their individual clients teaching them basic community living skills, escorting and introducing them to services and resources in the community, and acting as a liaison to gain the understanding and support of neighbors and local merchants for their clients. This program was highly successful in facilitating clients' adjustment to the community and is an example of the way that case manager functions can be extended and provided more intensely through the use of specialized ancillary staff.

Another important case management function is *crisis intervention.* The need for this type of support is particularly critical for those clients whose abilities to cope with living stresses are impaired or deficient. For example, the adjustment to community living made by many formerly institutionalized psychiatric patients is quite tenuous. Significant crises may be precipitated by unexpected changes in the environment, even events that seem trivial to persons with a "normal" level of coping ability. If such crises are not managed in a timely fashion, they can easily lead to significant deterioration in clients' levels of functioning and perhaps to their rehospitalization.

Because of their frequent ongoing contact with clients, case managers are likely to encounter such crisis situations. At the minimum, they must be prepared to provide clients with personal support. However, case managers need not be expected to function as therapists or to assist their clients directly in resolving the crisis. Instead, it may be more appropriate for them to refer or accompany the client to a crisis intervention team or agency.

Individual client advocacy is yet another important case management function, since some agencies may be resistant to providing entitlements or services to chronically disabled persons. In many situations such barriers can be overcome by the case manager through informal interpersonal negotiation (Riffer and Freedman 1980). However, in more difficult cases it may be necessary for case managers to enlist the support of supervisory or administrative level staff within their own agency or even to make use of more formal channels to advocate for clients. This may involve seeking the assistance of legal aid services or of agencies that traditionally provide advocacy services for clients in need (e.g., Mental Health Associations, Associations for Retarded Citizens). In fact, because of administrative barriers and conflicts of interest, citizen groups and legal advocates rather than formal service providers are often in the best position to provide certain types of advocacy (Governor's Interagency Task Force 1979).

Thus, while individual client advocacy is an important case management function, it cannot be delegated solely to case managers. As with other functions, there may be a need to involve other levels of agency personnel or specialized providers of services in order to provide clients with the degree of support required.

A final case management function to be considered here is *sys-*

tems level advocacy. In the course of trying to assure that clients receive continuity of care, it is inevitable that case managers will identify gaps in the service system. In other words, the system to which they are attempting to link their clients is likely to be incomplete. Needed services will simply not be available. The role of case managers in such a situation is, at a minimum, to document the gap and make their supervisors aware of the situation. However, there is a need for more direct action if the situation is to be alleviated. This is another example of a case management function that must involve key actors in addition to case managers. The intervention that is required to develop new service resources must take place on a systems level.

In order to facilitate systems level change it may be appropriate for case managers to begin by banding together not only to document the unmet need as a group but to act as a catalyst stimulating others to act (Horejsi 1978). These others may be the group of clients who have a similar unmet need or the agencies that may be responsible for planning, funding, and implementing the needed services within the locale. If continuity of care is to be provided to clients, case management activities must take place at many levels within the system.

Thus far, this discussion of structures needed to provide effective case management has focused primarily on just one element, the case manager. The individual in this role has the responsibility for the coordination of services at the individual client level. While this level of coordination is essential, the effectiveness of the case manager's efforts is constrained by the degree of support provided for case management at higher levels within the system. Thus, in order for a case management system to operate effectively there must be other formal structures for assuring coordination and linkage of services on a systems level.

Core agencies. Although there are many possible approaches for assuring the systemic integration of services for given target populations, almost all of these involve the allocation of special coordinating power and authority to a specified agency at the local level. The President's Commission on Mental Health (1978, p. 65), for example, recommended that "state mental health authorities, in consultation with local authorities, designate an agency in each geographic area to assume responsibility for assisting the chronically mentally ill from that area." Consistent with this suggestion, NIMH, in its contracting for the development of community support systems, expects state mental health agencies to specify a "core CSS agency" in each planning area to act as a convenor and catalyst in assuring that the comprehensive needs of the CSS population are met. More specifically, this core agency is responsible for the assessment of the needs of the CSS population, the negotiation of the interagency linkages and agreements necessary to provide all needed support services including case management, and the development of new service components to remedy any gaps in the existing service network (Turner and Shiffren 1979).

The importance of establishing this type of structure as part of an effective case management system cannot be overemphasized. One of the major lessons learned from services integration efforts thus far has been that compliance with the coordination efforts of case managers depends on a formal set of contracts that bind providers to deliver specified services to case-managed clients (Mittenthal 1976; Ross 1980). The core agency for a given locale is the most appropriate negotiator of such contracts. However, it can negotiate and implement such agreements effectively only if it has real enforcement power. Such power can result from the control of funds to purchase services from other providers, legislation or guidelines that require providers to respond to case manager requests, or the core agency being designated to serve as the single entry point into the entire local provider system.

Another important role that can be played by a core agency is to take responsibility for the development of new service components. While a major function of case managers is to link clients to services, they cannot perform it effectively if needed services do not exist. Thus, one of the very real constraints that case managers face is the adequacy of the service system in which they operate. If the system needs to be moved, a core agency is likely to be a far more effective change-agent than is the case manager. Nevertheless, even a core agency is unlikely to function effectively in this role unless it is explicitly empowered with the authority or responsibility for local system development.

Summary. Case management is a complex function. If effective continuity of care is to be provided for clients, coordination must take place at many levels within the system. Among the many possible structural elements that could be developed to implement case management, two have been specified as essential. The first is the case manager who provides coordination and integration of services at the client level. The second is the core agency which is responsible for coordination and linkage of programs at the local systems level. The specific details that must be considered when implementing the overall case management system are considered below.

Case Management Implementation

Systems Level Issues

Federal. In order for case management systems to function effectively, they need to be supported at all levels of governance within the service system. The federal level has already expressed clear support for the development of coordinated case management services for mentally disabled individuals. For the chronically mentally ill, federal support for the case management concept has taken the form of financial support of NIMH Community Support Program demonstration efforts, all of which have case management as a key service component. Further, as already discussed, federal support for the provision of case management services to the developmentally disabled has actually taken the form of a legislative mandate (PL 95-602). Ultimately, however, it is up to the states to respond by designing and actually operationalizing case management systems.

State. At the state level, the first step that needs to be taken in building a case management system is to fix responsibility for the program in a single agency of state government. Organizational structures for case management systems must be statewide in order to ensure uniformity and equity in the services delivered to those in need (Lippman 1976). However, the decision of which agency should assume responsibility and authority for providing case management services to the mentally disabled will vary from state to state.

In states that have separate departments to serve particular subgroups of mentally disabled persons, it is generally preferable for case management to be provided by the department most familiar with the given target population. However, since effective case management systems inevitably require the cooperation of all providers of human services, such a lead agency must coordinate its efforts with the activities of other specialized departments within state government. In New York State, for example, the Office of Mental Health has played the lead role in developing and managing the Community Support System (CSS) services that are being provided to chronic psychiatric patients living in the community. However, the Governor's Interagency Task Force has been formed to bring together the various human service departments that relate to CSS clients in order to enable them to serve these clients better.

One subcommittee of this task force deals specifically with case management services since they are such an essential component of the overall system. This subcommittee comprises representatives from the Office of Mental Health, Department of Social Services, Office of Vocational Rehabilitation, Office for Aging, and Office of Mental Retardation/Developmental Disabilities.

> Its purpose is to improve the practice of case management functions, finding out which agencies are currently fulfilling those functions and making recommendations which will reduce duplication and enhance efficient and effective delivery of case management services to CSS clients. [Governor's Interagency Task Force 1979, p. 1]

Such an interagency coordinating body is essential when case management services are delegated to an agency that serves just a particular population or provides only specific service functions. However, the need for such a mechanism may be somewhat less in those states in which the total responsibility for providing human services is assigned to a single, generic agency. Clearly, the nature of the existing human services organizational structure at the state level will be the primary determinant of how case management efforts are organized and administered. Nevertheless, it is also possible to alter organizational structures for case management purposes.

One example of such an alteration would be to create a totally new generic state level agency whose sole responsibility is the case management of human services clients. This model offers the advantage of avoiding a potential conflict of interest by separating case management from the provision of services. However, it may result in a style of case management that is not as individualized to clients as that which could be provided by agencies intimately familiar with the specific needs of their specialized target groups. In addition, the fiscal expenditures required for the creation of an entirely new department are likely to be substantial. Given the current climate in which resources for human services are shrinking, it is thus probably more realistic to build case management systems into the structures that presently exist.

Local. Regardless of the option that is chosen, once a state level agency has assumed responsibility for case management of a particular client population (e.g., mentally ill, developmentally disabled), this agency must then develop a plan for fixing the responsibility of case management in selected agencies at the local level. The primary consideration in selecting these agencies is that there be a single agency defined as responsible for each geographic subarea of the state. Further, since these "core agencies" provide the primary responsible mechanism for service integration within their regions, they must be chosen on the basis of their demonstrated leadership capacity.

Most case management programs have encouraged flexibility in determining the types of agencies that should assume the leadership role at the local level. The core service agencies designated for the NIMH Community Support Program developed for the chronically mentally ill vary from public hospitals to community mental health centers, to county social service agencies (Turner and Shiffren 1979). Core service agencies designated to serve this same population in New York State include county departments of mental health, general county hospitals, family services agencies, and even state psychiatric centers. The regional centers that provide case management services to mentally retarded persons in California include existing service or advocacy organizations, hospitals, and some nonprofit corporations developed specifically to assume the coordination role played by a regional center (Lippman 1976). The use of different models for the core agency is an important feature of case management systems since the factors that contribute to an agency's effectiveness in the leadership role vary greatly from one locale to another.

While the agencies assigned the core agency role may have no problems in exercising leadership, it is a good idea to provide formal mechanisms to facilitate their coordinating efforts. The most essential of these is to provide them with "purchase of service" power so that they can more easily gain the cooperation of a variety of the local human service agencies in providing services to clients served by the case management system (Washington, Karmen, and Friedlob 1974; Ross 1980).

In addition, the use of a local level counterpart to the state level interagency task force described above might be considered. More specifically, local interagency cooperation could be facilitated if the core agencies were to form interagency committees comprised of those agencies within their area whose services would be required in order to meet the comprehensive needs of clients (New York State Office of Mental Health 1978). Such a local interagency committee could be a useful forum for negotiating which roles would be performed by whom and for identifying gaps in the services available to the target population of interest. Thus, the core agency can use this committee to strengthen its capacity for carrying out its charge to provide comprehensive coordinated services to clients and to ensure that the entire range of services needed by clients is available.

Another method for strengthening the capacity of local core service agencies to coordinate care for clients is to designate these agencies as the single entry point into the service system in their geographic areas. This, in fact, is a model that has been used for serving the mentally retarded in California (i.e., Regional Centers) and that was recommended for use in serving the developmentally disabled in New Jersey (Lippman 1976). The model has distinct advantages over that of a core agency which must rely on multiple outside agencies to refer the clients who are eligible for or in need of case management.

One final consideration is crucial in the development of a statewide case management system and requires coordination between planners at the state and local levels. This consideration regards the completeness of the various local service systems within which case managers must work. Since case management is primarily a service linking and coordination function, its impact ultimately depends on the availability of the needed services. If some clients need to live in a supervised residence in order to adjust successfully to the community, and no such residences are available, providing them a case manager will not solve their problem. Although case management can assist clients in getting the maximum continuity of care available from a given service system, case management cannot be expected to be a sufficient intervention in a system which is missing fundamental direct service components. Thus, the development of needed services must, in some cases, precede or at least be contemporaneous with the development of a case management system if it is to operate as intended.

Client Level Issues. Just as core agencies are responsible for service coordination at the system level, case managers are responsible for integration at the client level. In most cases, it is probably a good strategy for case managers to be a part of the core agency. Provided that the core agency has been given adequate authority and power, this close relationship enhances the ability of case managers to gain the cooperation of other service providers within the area. However, for a variety of reasons, some core agencies may choose to contract with another local service agency to provide case manager services. For example, this might be a good strategy for avoiding a potential conflict of interest when the core agency itself is a major provider of direct services to clients.

Regardless of where case managers are located, they are the key to the quality and the effectiveness of any case management system. While core agencies may provide the support and authority to facilitate interagency coordination, it is the individual case managers who must interact with a wide range of individual service providers in order to make the coordination actually take place for individual clients. Given the centrality of the role of the case manager in case management systems, it is important to consider how various aspects of the job design and context affect case manager effectiveness.

Case Manager Status. Perhaps the most essential aspect of the job design of the case manager role is the status that the case manager is given. One question frequently raised in this regard is whether the case manager should be a professional or a paraprofessional level worker. Since the demarcation between these two categories may vary from one human services discipline to another, however, it is probably more useful to discuss specific aspects of individuals' preparation for the role, including their educational background and previous job experience.

The important aspects of educational background are the type and level of academic degree obtained. In general, case managers have typically been individuals with education in a human services field. Some persons would suggest, however, that training in some human service disciplines may be more relevant to the case manager role than that of others. For example, individuals who have been trained to be aware of how to use various providers of human services in order to meet clients' needs (e.g., social workers, human service generalist workers) are likely to be better prepared to act as case managers than persons whose training has been focused primarily in a given discipline (e.g., psychology).

In addition to type of education, however, there is also the factor of level of education. The educational level reported for case managers in various programs described in the human services literature ranges from high school diploma (McPheeters 1974) to doctoral degree (Altshuler and Forward 1978). Depending on what is expected of the case manager, individuals anywhere within this range can function effectively.

The impact of level of education on job functioning will also interact to a great degree with the specific job experiences of the individuals involved. For example, case managers for chronic psychiatric patients in New York State include both persons who do not have college degrees but who have had extensive experience in working with these patients in state psychiatric facilities and persons who have masters level degrees in social work or counseling but who have had no prior contact with chronic psychiatric clients (Baker, Jodrey, and Morell 1979). Clearly, each type of worker brings different strengths to the case manager's role. Which strength is more important is not clear, since there is empirical evidence that level of education and number of years' experience in the specific problem field both seem to strengthen case manager effectiveness (Berkeley Planning Associates 1977).

In most systems, case managers are required to have no more than a B.A. level degree, which affords them a paraprofessional status. This fact has a number of consequences. First, it limits the range of activities that case managers can perform without supervision. In addition, due to their paraprofessional status case managers may have difficulty in establishing credibility with the professionals to whom they must relate in coordinating client care. While there is some evidence to suggest that the case managers can effectively resolve this problem over time (Baker, Intagliata, and Kirshstein 1980), they may occasionally require additional backing and support from their core agency.

Because of these problems, some program administrators might feel that it would be better to use professionals for the case manager role. However, while professionals may be capable of functioning more independently as case managers, they are likely to be unwilling to devote time to many of the important but "less professional" services which paraprofessional case managers frequently provide to clients (e.g., transportation to an appointment, assistance in filling out forms to secure entitlements, visiting a day program to observe client activity). For example, Caragonne (1981) found that many case managers in mental health settings spent extensive amounts of time providing direct services to clients (e.g., counseling, assessment) and neglected such key case management functions as linking, referral, followup, and evaluation. Further, since professionals are overqualified for many important case manager duties, they may "burn out " more quickly than paraprofessionals (Dormady 1980). Finally, an important economic consideration is that the use of professional level case managers would greatly increase the costs of any sizable case management effort.

These various considerations would suggest that the most cost-effective alternative may be to hire paraprofessionals to perform the essential case manager functions of linking and monitoring. The other important case management functions of assessing and planning could be performed by these individuals to the extent to which they are capable but should ultimately be the responsibility of professional level clinician supervisors. Before making any final decisions regarding the degree of discretion and authority that paraprofessional case managers should be given in their activities, however, it should be noted that case managers attach great importance to autonomy in their jobs (Caragonne 1980). Further, their job satisfaction reportedly increases as they are given greater freedom and discretion in carrying out their role responsibilities (Graham 1980). There is no evidence that one particular level of autonomy is ideal, but it is advised that the degree of autonomy given to case managers must be matched to the expectations that were established when they were recruited for the role and that it be adjusted over time to reflect their increasing competence

Training/Preparation. The development and implementation of a case manager training program should be viewed as an essential component in the building of any effective case management system. Regardless of the professional level of the individuals being hired as case managers, it is important that they approach their role with a clear understanding of their functions and responsibilities. Further, in order to provide a consistent and equitable statewide case management program, it is important that all case managers be given similar orientation and preparation for the job.

In considering the development of a statewide training package for case managers, it is essential to build in a great deal of flexibility in its implementation. The people who will be assuming the case manager positions will undoubtedly vary widely in the knowledge, skills, and competencies that they bring to the job. A useful strategy is to design a training program as a series of self-contained learning modules (Baker, Jodrey, and Morell 1979). In this way, those trainees who can demonstrate their preparation in a given area need not complete that specific module.

The statewide training package should focus on the basic aspects of the case manager role. It should include modules that present the rationale for the case management process and make explicit the values that are intended to guide the activities of case managers. These are modules that should be required for all trainees regardless of their prior job experience. Additional modules should provide basic information in such key content areas as the nature of mental illness or mental retardation (e.g., causes, definitions, associated consequences, limitations), common medications and their side effects, the local availability of specific services and the entire range of available client entitlements (e.g., SSI, food stamps), clients' legal rights, and the recordkeeping responsibilities of case managers. Training should also include modules that deal with the process of case management. These should focus on teaching case managers skills for relating to clients, setting goals, solving practical problems, knowing how and when to intervene in crisis situations, and advocating effectively for clients.

In training case managers for working with chronically mentally disabled clients, it is also important to help trainees appreciate that the nature of the disabilities of many of their clients will severely limit their ability to progress behaviorally. Lamb (1979) has noted that unless staff who work with this client population have a realistic conception of what they can expect to accomplish, staff frustration and burnout are inevitable. Case managers must accept that enhancing the quality of clients' lives rather than increasing their level of independent functioning is a reasonable and appropriate treatment goal for this population.

In addition to considering the training content, it is also important to consider how the training can be implemented most effectively. One suggestion made by several authors who have evaluated case manager training programs is that care should be taken to avoid assigning complete caseloads to case managers until they have completed their training (Amadio 1976; Baker, Jodrey, and Morell 1979). While it is useful to have some actual client responsibilities during training so that trainees can apply what they are learning, there are indications that too much client responsibility interferes with learning. To avoid this problem, it may be desirable to conduct training intensively over a short period rather than to extend it in small segments over a longer period.

A final consideration is that while a basic statewide training program should be developed to prepare case managers for their role, plans should also be made to provide continuing education to case managers. An initial time-limited, intensive training program simply cannot be expected to meet all case managers' training needs. As with most positions, case managers will not really know what they need to know until they have been on the job for a while. Thus, either at the state or local level, continuing education sessions should be planned. Further, case managers themselves should be assessed periodically in order to determine the most important areas of training need so that continuing education sessions remain relevant and useful.

Supervision. The type and extent of supervision that is appropriate for case managers depends upon the range of functions that they are assigned and on the level of individual selected for the role. If experienced professional level case managers are hired, they certainly will not require the extent of supervision appropriate for a paraprofessional or less experienced individual in the same role. However, since most programs are likely to use paraprofessional level persons to fill this challenging role, it is extremely important to plan to provide them with adequate support and supervision.

Those assigned as case manager supervisors should perform several important functions. First, they must monitor the performance of case managers in a thorough, ongoing fashion. In addition to meeting regularly with individual case managers to discuss their caseload activities, it may be useful for supervisors to observe or even assist their case managers in working with certain clients. While one might assume that case management supervisors in all settings would routinely conduct such activities, the findings of Caragonne (1981) suggest otherwise. Specifically, she reported that many of the supervisors and program administrators at the 22 case management sites studied did not have accurate perceptions of the scope, extent, and pattern of their own case managers' activities. Further, it was exactly in those sites where supervisors were most out of touch with their case managers' activities that the case managers departed most drastically from their defined roles.

A second important aspect of the supervisory role is the staff development function. Supervision should include an ongoing commitment to the continuing education of case managers. Part of this education might be informal and consist of something as simple as encouraging case managers to develop a habit of generating multiple alternative strategies for dealing with clients' problems before taking action. However, it is also appropriate for supervisors to consider providing some more formal continuing education sessions to case managers. These sessions can be designed to be either didactic or experiential and should focus on specific content areas in which the case managers themselves feel a need for more background.

A third, and perhaps the most important, function of the supervisory role is to provide case managers with needed individual support. Graham (1980) found that the provision of consistent supervisory feedback and support to case managers of chronic psychiatric patients was associated with greater case manager work motivation. Apparently, case managers need such support in order to maintain an ongoing sense of the value of their work and the extent to which it is appreciated. Further evidence of the importance of providing supportive supervision to case managers has been provided elsewhere. Specifically, Baker, Intagliata, and Kirshstein (1980) reported that case managers identified regular supervision as an essential activity for preventing "burnout." They described good supervision as providing them with an opportunity to "vent their frustrations with their clients and the system" and to receive support for their efforts. Further, Caragonne (1979) found that case management sites where supervision consisted more of supportive, enabling activities rather than of monitoring and control were also the sites where case managers exhibited less antagonism toward management, lower levels of absenteeism and stereotyping of clients, and, in general, fewer overall symptoms associated with case manager burnout.

Clearly, the role of the case manager supervisor is a very significant one. Establishing such an upper level case management related position not only provides case managers with an opportunity to receive needed support and back-up, but also offers case managers the possibility of upward job mobility. While such a position would provide just part of a case management career ladder, any efforts along these lines enhance the likelihood of case managers remaining with the system after they have significantly increased their expertise.

Individual vs. Team Case Management. Those implementing the case manager concept for chronic psychiatric patients living in the community have indicated that comprehensive responsibility for clients might be more appropriately assigned to a case management team than to individual case managers (Gittelman 1974; Kirk and Therrien 1975; May 1975; Altshuler and Forward 1978; Turner and TenHoor 1978; Test 1979). This team comprise a group of individuals who, together, are responsible for the case management functions of assessing, linking, and monitoring to assure continuity of appropriate care to clients. The individuals on this team may all be case managers or might include a case manager along with a variety of professionals from different disciplines (e.g., psychiatrist, nurse, psychologist, social worker).

According to Test (1979), the advantages of a team structure are that it provides (1) more continuous coverage and coordination since the unavailability of a single case manager does not incapacitate the client; (2) better planning based on the availability of more points of view for managing difficult problems, a factor especially important for maintaining energy and creativity in working with chronic clients; and (3) a way to avoid the isolation that may lead to burnout of the individual case manager who must face tedious, seemingly endless, and emotionally draining problems alone.

A recent report on the case management efforts at one of the NIMH Community Support System demonstration sites in New York State provides some support for Test's (1979) position. Specifically, Reagles and Sheets (1979) reported that after a year of using the individual case management model to serve caseloads of chronic psychiatric patients, two significant problems had surfaced. These were the overwhelming burden of responsibility leading to staff burnout and the dysfunctional phenomenon of clients becoming overly dependent on case managers. In response to these problems the program has switched to a group case management model in which the ultimate responsibility for individual clients' care rests with an interdisciplinary team rather than one case manager.

While the team model of case management may not be appropriate or feasible in all programs, those using an individual case manager model must pay serious attention to the need to provide case managers with adequate support. If case managers are not included as part of an interdisciplinary treatment team, then it is essential that the case managers themselves be organized either formally or informally for the purpose of mutual support. One possibility is to designate them as a distinct formal organizational entity, the "case management unit." Whether or not such a unit is formed, there is a need to provide mechanisms that facilitate the regular interaction of case managers as a group. Examples would include daily morning meetings, weekly supervision sessions and periodic training sessions.

Caseload Characteristics. A major factor influencing the style and effectiveness of services offered by case managers is the number of clients for whom they are responsible. It is a simple fact that as the number of clients assigned to a given case manager increases, the amount of time the case manager can potentially devote to each individual client decreases. Graham (1980) confirmed this relationship in his study of case managers who were serving varying sized caseloads of chronic psychiatric patients in New York State. He reported that as caseload size increased, case managers *did not* increase the number of clients seen each week. Thus, the frequency with which individual clients were seen by case managers decreased with increasing caseload size. This relationship is extremely important to consider because there is evidence that the quality of case management services is strongly related to the intensity of contact between client and case manager (Berkeley Planning Associates 1977).

Increasing caseload size can affect not only the amount or frequency of case managers' contact with clients but also the nature and quality of client contact. In a study of case management being provided to chronic psychiatric patients, also in New York State, Baker, Intagliata, and Kirshstein (1980) indicated that the increase from caseload sizes of approximately 15 clients to as many as 30-50 clients had a significant impact on case managers' working styles. In addition to the inevitable consequence of having less time for each client, case managers reported that:

- Their efforts with clients had become primarily reactive rather than proactive such that the majority of their time was consumed responding to crises rather than anticipating problems and helping clients to plan ahead for them;
- They were always "on the run" and no longer had the chance really to get to know their clients and their needs;
- In order to save time, they had begun increasingly to do things for clients instead of helping clients become more independent;
- Their frequency of contact with clients was increasingly being determined by clients taking the initiative to contact them rather than vice versa (i.e. "the squeaky wheel gets the oil");
- The amount of time they were required to spend simply documenting their efforts with clients was consuming an increasingly alarming portion of their time that otherwise might be spent with clients.

Clearly, these are troublesome developments that potentially, if not immediately, threaten the quality and effectiveness of their case managers' efforts.

Undoubtedly, caseload size is an extremely important factor shaping case management. However, determining ideal caseload size is a difficult task. The number of clients that a case manager can serve effectively will vary depending on the mix of clients' levels of functioning (acute/chronic needs), the degree to which clients live close together or in scattered locations, and the competencies of individual case managers. Lannon (1979) reported that case managers serving chronic psychiatric patients tended to give more attention and service to those individuals who had poor community living skills or who exhibited behavior management problems. Graham (1980) indicated that case managers who serve specialized groups of clients tend to have different work patterns than those serving mixed caseloads. Specifically, he reported that case managers serving only psychiatric clients living in family (foster) care homes spent significantly less time in direct client contact than did case managers assigned a mix of clients living in varied community residential settings.

Clearly, a variety of client characteristics affect case management activities, independent of caseload size. However, it is useful to discuss at least estimates of reasonable caseload levels based on actual program experience. For chronic psychiatric patients being served in community support system programs in New York State, suggested estimates for an individual case manager's load have ranged from a low of 15 clients (Reagles and Sheets 1979) to a high of 30 (Baker, Intagliata, and Kirshstein 1980). On the other hand, those reporting the use of the case management team model for a similar client population describe team member/client ratios ranging from 1/4 (Test 1979) to 1/10 (Reagles and Sheets 1979).

Regardless of the client population being served, determining ideal caseload size ultimately depends on the type of case management that program planners intend to offer. If, for example, case managers are expected to provide clients with support only when they are in crisis, they may be able to handle caseloads of 40-50 clients. However, if case managers are expected to assess clients' needs, develop treatment plans, link clients to services, monitor clients' progress, attend to needs of clients' families, and update treatment plans in an ongoing fashion, caseloads of 20-30 clients are likely to be more appropriate.

The actual caseload size that is ideal for serving any client group should be determined on a program by program basis. Thus, as part of the planning for developing a case management program, it may be wise to set caseload sizes conservatively low at first and then, if all goes well, gradually increase them while monitoring the consequences. In this fashion, the decision to set fixed caseload sizes can be made more empirically and rationally.

Other Contextual Factors. There are two additional contextual factors that can have a significant impact on how case managers perform their functions. The first of these is the degree to which the existing range of services available to clients meet their comprehensive needs. A number of studies of case managers' activities (Caragonne 1979; Baker, Intagliata, and Kirshstein 1980; Graham 1980) have indicated that case managers' activities are significantly shaped by the service system in which they operate. If, for example, there are relatively few services available, case managers spend relatively little time linking clients to services. Further, when certain important support services are unavailable, case managers are likely to devote their own time either to providing or creating the needed services. These results are important for program planners to consider. They indicate that case managers' actual activities are shaped ultimately by the constraints of the environments within which they work, not by their formal job descriptions.

The other contextual factor that deserves consideration is that the local agencies that assume responsibility for providing case management in their respective regions are each likely to develop somewhat unique case management programs. Though efforts may be made at a state level to give programs essential structural and ideological uniformity, the implementation of these guidelines at the local level is ultimately shaped by the unique local contexts.

Factors that result in interprogram variation include the differences between regions in population make-up, geography, availability of support services, history of interagency cooperation and competition, and case management ideologies of the individual core agencies. Thus, a statewide case management effort typically comprises the activities of a variety of somewhat unique case management programs. While monitoring mechanisms to ensure a certain amount of program uniformity and equitable quality care for clients are desirable, local flexibility in program implementation should be not only tolerated but encouraged. This flexibility enables programs to be tailored to meet both local and individual needs.

Summary and Recommendations

The design, development, and implementation of a statewide case management program for the chronically mentally disabled is a complex task that requires the coordinated efforts of human services providers at all levels of the system. Consequently, the level of difficulty facing those charged with this task depends upon the degree to which the structures and actors within the system facilitate cooperation and collaboration. However, since the need for case management has resulted, at least in part, from the lack of coordination and cooperation within the system, the development of case management services will inevitably be hindered by significant barriers.

Perhaps the easiest solution would be to start over by designing, building, and installing a completely new human services system into which case management services could be neatly incorporated from the very beginning. Unfortunately, this is not a realistic option. Instead, planners must develop case management programs that can be "fit into" existing service systems. They must build upon the system components that provide potential for enhancing service coordination and continuity while working around those elements that create service fragmentation. In addition, some new mechanisms and structures for ensuring coordinated continuous care will need to be designed and implemented. In each case, the end result must be a case management program that reflects the unique strengths and needs of the system of which it is a part.

A number of suggestions and recommendations for the effective implementation of case management systems have been discussed here. The major considerations can be summarized as follows:

- The development of a case management system should begin with a thorough assessment of client needs and the service resources that currently exist to meet them. Plans must be made to begin to fill identified service gaps. Case management alone cannot be expected to solve the problems created by incomplete, inadequate service systems.
- The responsibility for providing case management services to a

given population of mentally disabled persons should be delegated to a single agency at the state level. If this agency specializes in serving this particular client group, steps must be taken to involve representatives from all other relevant human service agencies at the state level in the process of planning and implementing case management services.

- The agency responsible for case management services at the state level must delegate case management authority and responsibility to "core agencies" at the local level. These core agencies must be responsible for establishing interagency cooperation in their locales and for providing case management services. To create reliable human services networks in their regions, core agencies must be supported with formal mechanisms for enhancing cooperation (e.g., purchase of service authority, legislation).
- Case managers are the most important service providers in a case management system. While they do not perform all case management functions, they are the human link between the client and the system. They assure that clients are receiving all the services they need, in the amount and at the time they are needed. To function effectively, case managers must be provided with adequate training, supervision, and ongoing support.

Evaluation and Research Needed. To enhance the quality of case management services, there is also a clear need to give far greater attention to conducting systematic ongoing evaluation of and research on case management systems. Two types of evaluation efforts should be considered. In the early phases of program development, it is important that evaluation be conducted and focus on measuring program implementation. Information that is produced from this phase of evaluation can provide system planners with formative feedback that can be used to keep program development "on track" or to modify or reshape program design if deemed necessary. These process evaluation efforts should help to pinpoint how case management services are provided and the factors that seem to affect their delivery. This information is important if administrators or providers are to understand or replicate the results of any case management program.

Once case management programs are functioning as intended, it is appropriate for evaluators and researchers to shift their focus to measuring program outcomes or benefits. Examples of outcomes that should be studied include the extent to which the various objectives of case management services, described earlier in this article, have actually been met. These include enhancing the continuity and comprehensiveness of care, improving the accessibility of services to clients, and increasing the efficiency (i.e., cost effectiveness) with which needed services are provided.

In addition to assessing the extent to which case management enhances the effective functioning of an extant service system, it would also be useful to evaluate the impact of those direct services which case managers provide to their own clients, often as a means of filling in gaps in the service system. Further, since as described previously, the case manager is the important *human* connection between the client and the system, it would be useful to assess how having such a personal advocate affects clients' feelings about themselves and their responsiveness to the services to which their case managers link them.

In addition to evaluating a number of aspects of the process and outcome of case management, there is also a need for research to determine how a large number of important contextual variables exert their influence on both case management processes and outcomes. In general, these factors can be grouped into four major categories. The first category includes the individual characteristics that case managers bring with them to their jobs. These characteristics include age, level of education, relevant work experience, and their expectations about the job. A particular research question that should be addressed regards the relative influence of case managers' education, experience, and personal qualities on their work activity patterns and overall effectiveness.

The second category of variables includes the characteristics of the clients who are served. These characteristics include age, functional skill level, level of maladaptive behavior, institutionalization history (degree of chronicity), and current diagnosis and symptomatology. Important research questions in this category relate to how client characteristics affect the frequency of case manager contact, the total amount of case managers' time expended, and the specific nature of the assistance which case managers provide to their clients.

A third category of variables comprises the characteristics of the case managers' job design and work environment. These characteristics include the breadth of role responsibilities, degree of job autonomy, size of client caseload, the individual vs. team model of case management, and the type and quality of supervision provided. One important researchable issue in this area is the optimum number and types of disabled persons in a caseload. Other important research questions relate to identifying the factors that enhance work motivation, reduce burnout, and increase overall job tenure and effectiveness among case managers.

A fourth and final category comprises characteristics of the broader services network within which case managers must function. These characteristics include the degree of service availability, the extent of interagency cooperation, and the type, if any, of core agency functioning within the locale. Important research questions in this area involve the assessment of how the extent of cooperation and connectedness between key agencies influences the case management process and what types of core-agency models work best to enhance case management effectiveness.

A number of exploratory studies (Lannon 1979; Baker, Intagliata, and Kirshstein 1980; Graham 1980; Ross 1980; Caragonne 1981) of factors that affect case managers' activities and effectiveness have already been conducted, and their results have been discussed elsewhere in this article. However, much important research remains to be done. Each of the categories of variables described deserves more extensive attention and a variety of research methods can prove useful. These include case study approaches as well as experimental and quasi-experimental designs. Further, to gain a better overall sense of the relative importance of and interactions between the major categories of variables outlined, complex multivariate research designs will eventually be required. Nevertheless, ongoing work in this area is essential. Without solid empirical information on case management, program development can only continue to take place in a haphazard fashion.

The importance of research on case management should not be minimized. Given the present economic and political climate in which available funding for human services programs is shrinking significantly, case management programs will be particularly vulnerable since they provide indirect services to clients. If a choice has to be made between using funds for case managers or for work skills training programs for clients, it is likely that the more direct client services will be funded. Thus, if case management programs are to remain viable in the 1980s, it is crucial that program administrators have the information that is needed to demonstrate their value and effectiveness.

The development of case management systems is an ambitious undertaking. However, there is good reason to believe that the outcome will be worth the effort. Evaluations of service integration projects have reported that the use of case teams and case manager linkages leads to increases in the accessibility, comprehensiveness, and volume of services provided to clients (Baker and Northman 1981). Caragonne (1979) came to similar conclusions and, in addition, reported that the use of case managers led to more effective packaging of client service plans, documented gaps and duplications in service networks, and generally promoted organizational responsiveness to consumer needs. Although this evidence is encouraging, it is important to acknowledge that many questions about the most effective methods for providing case management services remain unanswered. At present, like many aspects of the human service field, case management is more art than science. Thus, as we proceed to implement case management systems for the chronically mentally disabled, we must remain open to learning and change.

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Bibliography and Abstracts on Schizophrenia

The abstracts that appear below are drawn from the computer-based information storage and retrieval system operated by the National Clearinghouse for Mental Health Information. They were selected for inclusion here on the basis of their direct relevance to schizophrenia: judgments about the quality of the article or book abstracted have been left to the reader. Foreign titles have been translated and the city of the journal's origin noted. Languages that use neither the Latin nor Fraktur (German) alphabets (e.g., the Slavic languages) have been transliterated. Titles of articles, books, and infrequently cited journals have been translated from these languages, and all other identifying information appears in English in their citations.

This collection is not exhaustive. The Clearinghouse routinely scans all mental health related literature, and its information system includes references to a great many articles of potential use to readers who are involved with research, training, or treatment in schizophrenia. Many of these references—notably reports of basic research—may not be published in the *Bulletin,* but are available from the Clearinghouse in other publications or through individually generated bibliographies. Because *Psychopharmacology Abstracts* publishes a comprehensive list of new articles on drug trials in schizophrenia monthly, only those articles that review a number of psychopharmacological studies are published here. Mental health professionals or laypersons actively working in the mental health field who wish to request computer printouts of late references or comprehensive bibliographies on specific aspects of schizophrenia may write to the following address: Technical Information Section, National Clearinghouse for Mental Health Information, National Institute of Mental Health, Rm. 11A21, 5600 Fishers Lane, Rockville, MD 20857.

The articles described in these abstracts are not available from either the Clearinghouse or the Center for Studies of Schizophrenia.

Attention, Perception, and Cognition

4537. Ando, K.; Moriya, H.; Toyota, T.; Kojima, T.; and Shimazono, Y. (Department of Neuropsychiatry, Tokyo Medical and Dental University, Tokyo, Japan) Visual perception process in chronic schizophrenia and endogenous depression. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. B. Amsterdam; Elsevier/North Holland, 1979. pp. 1472–1477.

The visual fixations of chronic schizophrenics, their relatives, endogenous depressives, and normals were measured by viewing two pictures. Number of eye fixation points in schizophrenics and their relatives was significantly less, and mean fixation time was significantly longer than that in normals. A similar performance occurred in depressives. In normals and depressives the number of fixations and total distances of scanning paths increased, and mean fixation time decreased after instructions were given to view the picture more carefully. However, chronic schizophrenics and their relatives showed no significant changes. Less frequent eye fixation in depressives was closely correlated with two items of Hamilton's rating scale—retardation of decline in work and interests. The patients who were socially recovered from the depressed state showed significantly improved performance. (4 references)—Author abstract, modified.

4538. Johnston, M.H., and Holzman, P.S. (Child Psychiatry Clinic, University of Illinois Medical Center, Chicago, IL 60612) Assessing Schizophrenic Thinking: A Clinical and Research Instrument for Measuring Thought Disorder. San Francisco: Jossey-Bass, 1979.

The validation of the Thought Disorder Index (TDI), a scale for classifying language peculiarities in the Wechsler Adult Intelligence Scale (WAIS) and Rorschach protocols, is described. The TDI classifies abnormal verbalizations into four levels of severity. The subjects included acute and chronic schizophrenics, nonschizophrenic psychotics, nonpsychotic psychiatric patients, relatives of the schizophrenics, and normal controls. The subjects were also measured on IQ, paranoid status, premorbid adjustment, and global severity of pathology. It was found that the language peculiarities measured by the TDI occur in nonschizophrenics and other psychiatric patients. The results indicate that there is to be a continuum, in terms of both frequency and severity, with schizophrenics at one end and normals at the other.

4539. Phillips, W.M.; Phillips, A. M.; and Shearn, C.R. (Institute of Living, 400 Washington St., Hartford, CT 06106) Objective assessment of schizophrenic thinking. Journal of Clinical Psychology, 36(1):79–89, 1980.

The relative effectiveness of a number of highly structured testing procedures, accepted clinically as possessing some validity in the detection of schizophrenic thinking, were examined. The Whitaker Index of Schizophrenic Thinking, Shipley-Hartford Intelligence Scale, Gorham Proverbs Test, Goldstein-Scheerer Object Sorting Test, and the Similarities and Comprehension subtests of the Wechsler Adult Intelligence Scale were administered to 36 nonschizophrenic and 23 schizophrenic patients. Results indicated that moderate relationships were found among three of the five techniques, independent of whether they measured general or specific deficit, active or passive thinking, and/or positive or negative symptoms. Discriminant analysis indicated that the most accurate and economical combinations of techniques in the differential diagnosis of schizophrenic thinking, for a homogeneous, mildly to moderately impaired hospital population, would be a combination of a measure of generalized deficit and a measure of positive symptoms. (16 references)—Author abstract, modified.

4540. Place, E.J., and Gilmore, G.C. (Department of Psychology, Case Western Reserve University, Cleveland, OH 44106) Perceptual organization in schizophrenia. Journal of Abnormal Psychology, 89(3):409–418, 1980.

A report of numerosity task was used in two experiments to examine the effect of inherent stimulus organization on the report accuracy of two schizophrenics and controls. Displays containing from zero to six lines were presented tachistoscopically. In Experiment 1, the lines appeared either alone or with noise elements—circles. When the lines appeared alone, the groups performed comparably. In Experiment 2, the stimulus arrays did not contain noise elements, and subjects were to report all the lines they saw. The performance of controls deteriorated as the organization of the arrays became more complex. The schizophrenics were not affected by the organization variable, and their average performance was significantly better than that of controls. The results of both experiments suggest that the schizophrenic perceptual deficit may be a failure to organize information at an early stage in processing. (24 references)—Author abstract, modified.

4541. Plumer, J.A. (Case Western Reserve University, Cleveland, OH 44106) Correlates of self-nonself boundary disturbance in schizophrenia: A construct validity study. Dissertation Abstracts International, 40(12):5827–B, 1980.

The correlates of self/nonself boundary disturbance in three areas of psychological functioning—social maturity, cognitive/perceptual functioning, and interpersonal orientation—were investigated using Fisher and Cleveland's Rorschach body image boundary scoring system with a sample of 50 hospitalized schizophrenic patients. It was hypothesized and confirmed that level of self/nonself boundary stability correlates with level of social maturity as measured by the Ullmann/Giovannoni process/reactive questionnaire and level of cognitive/perceptual articulation as measured by Rorschach Genetic Level scores. The hypothesized relationship between self/nonself boundary stability and interpersonal orientation measured by MMPI dependency scale scores was not confirmed.—Journal abstract, modified.

4542. Simpson, G.B.; Bourne, L.E., Jr.; Justesen, D.R.; and Rhodes, R.J. (Department of Psychology, University of Kansas, Lawrence, KS 66045) Schizophrenic and paranoid thinking in conceptual performance. Bulletin of the Psychonomic Society, 13(2):97–100, 1979.

To determine whether the identification of critical stimulus attributes differs among chronic schizophrenic patients when there is an overlay of paranoid thinking, 32 hospitalized schizophrenic patients were assigned in equal numbers to four groups on the basis of scores on the Whitaker Index of Schizophrenic Thinking (WIST) and the paranoid (Pa) scale of the Minnesota Multiphasic Personality Inventory (MMPI). Subjects attempted to solve two concept transformation problems in which they were to identify relevant stimulus attributes under two levels of demand of their memories for previous stimuli. Only in conjunction with a low score on the Pa scale did the schizophrenic index predict a conceptual deficit. Only the high WIST, low Pa group differed significantly from a control group of normal subjects. This result qualifies earlier research concerning the power of the WIST to predict logical performance. No difference was found between the two levels of memory demand. (11 references)—Author abstract, modified.

4543. Tomer, R.; Mintz, M.; Levy, A.; and Myslobodsky, M. (Psychology Research Unit, Tel Aviv University, Sharett 109, Ramat Aviv, Israel) Smooth pursuit pattern in schizophrenic patients during cognitive task. Biological Psychiatry, 16(2):131–144, 1981.

Asymmetries in saccadic pursuit were studied during an interview and during a cognitive task in 20 schizophrenic inpatients and 25 controls, screened for their patterns of lateral eye movements (LEM). Patients were poor trackers, but no asymmetries were observed during the interview. However, solving syllogisms while tracking resulted in further deterioration in tracking performance of the patients, with significantly more saccades and arrests in tracking occurring when following the target to the left as compared to the right. Similar asymmetry was observed in one group of controls, who were believed to rely more on the left hemisphere on the LEM test than did the second control group. These results support the hypothesis of left hemispheric hyperreactivity in schizophrenia. Saccadic pursuit in the first control group suggests that these subjects may be at high risk. (30 references)—Author abstract, modified.

4544. Zahn, T.P. (Laboratory of Psychology and Psychopathology, NIMH, Bethesda, MD 20205) Predicting outcome from measures of attention and autonomic functioning. In: Baxter, C., ed. Perspectives in Schizophrenia Research. New York: Raven Press, 1980. pp. 81–106.

To support the thesis that attention and autonomic nervous system (ANS) activity should be measured more often in clinical studies of schizophrenia, evidence is presented which suggests that attention and ANS functioning may be partly biologically determined traits with etiological and prognostic significance. New evidence is reviewed on: (1) the relationship of measures of attentional and autonomic functioning to subsequent clinical course (i.e., outcome) in both unmedicated patients and those taking antipsychotic drugs; (2) changes in psychophysiological functioning in relation to clinical changes—changes which occur in unmedicated patients are compared to changes attributable to drugs; and (3) other relevant evidence on possible genetic and neurochemical determinants of the attentional ANS deficits in schizophrenia. The data suggest that ANS activity is related to biogenic amines and to enzyme activities which are thought to play important [illegible] in schizophrenia. The discussion that followed the presentation of the paper at a symposium on strategies for future research in schizophrenia is given. (61 references)

Biology

4545. Baastrup, P.C.; Christiansen, C.; and Transbol, I. (Glostrup Hospital, DK-2600 Glostrup, Denmark) Calcium metabolism in schizophrenic patients on long-term neuroleptic therapy. Neuropsychobiology, 6(1):56–59, 1980.

The bone mineral content (BMC) in both forearms—e.g., highly related to total body calcium—was measured in a large group of schizophrenic patients receiving neuroleptic drugs. The mean BMC value was 86 percent of normal, and the decrease was independent of the type of neuroleptic treatment. In contrast, the biochemical variables—serum calcium, magnesium, phosphate, and alkaline phosphatases—were virtually normal. This combination of osteopenia and normal biochemical variables suggests that schizophrenics have osteoporosis, either due to the disease or to the treatment given. (7 references)—Author abstract, modified)

4546. Berger, P.A.; Faull, K.F.; Kilkowski, J.; Anderson, P.J.; Kraemer, H.; Davis, K.L.; and Barchas, J.D. (Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305) CSF monoamine metabolites in depression and schizophrenia. American Journal of Psychiatry, 137(2):174–180, 1980.

The cerebrospinal fluid (CSF) concentrations of five monoamine metabolites were examined before and after probenecid administration in normal subjects and in patients with depression and schizophrenia. No differences occurred in baseline metabolite concentrations among the three groups. CSF metabolite and CSF probenecid concentrations were significantly correlated in depressed subjects for all metabolites, while decreased postprobenecid accumulation of homovanillic acid occurred in these subjects as compared with other groups. A method for correcting for probenecid concentrations is proposed, and it is concluded that data from normal subjects will be valuable in future research using the probenecid technique. (49 references)— Author abstract, modified.

4547. Buchsbaum, M.S.; Davis, G.C.; and van Kammen, D.P. (Biological Psychiatry Branch, NIMH, Bethesda, MD 20205) Diagnostic classification and the endorphin hypothesis of schizophrenia: Individual differences and psychopharmacological strategies. In: Baxter, C., ed. Perspectives in Schizophrenia Research. New York: Raven Press, 1980. pp. 177–194.

The endorphin hypothesis of schizophrenia is reviewed as a case history of research, as a target for psychophysiological and neuropharmacologic approaches, and as a potentially viable but limited factor in mental dysfunction. Direct evidence for the endorphin hypothesis, indirect evidence—pain sensitivity, electrophysiological measures of sensory sensitivity, and opiate antagonists and evoked potential amplitude—for a role of endorphins in schizophrenia, and specificity of pain insensitivity findings for schizophrenia are discussed, and new strategies for identifying subgroups of schizophrenic patients are considered. The discussion that followed the presentation of the paper at a symposium on strategies for future research in schizophrenia is given. (62 references)

4548. Bucht, G.; Gottfries, C.G.; Roos, B.-E.; and Winblad, B. (Department of Medicine, University of Umeå, Umeå, Sweden) Reduced concentration of 5-hydroxytryptamine in brains from demented schizophrenic patients. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 381–388.

Post-mortem investigation of brains from 12 schizophrenic patients was performed to study concentration of 5-hydroxytryptamine (5-HT) and the metabolites 5-hydroxyindoleacetic acid (5-HIAA) and homovanillic acid (HVA). The concentrations of catecholamines and HVA in different parts of the brain in schizophrenic subjects did not differ from those in controls. Concentration of 5-HT in schizophrenic brains was consistently low and in some areas was significantly lower than controls. Concentration of 5-HIAA was discovered only in a few schizophrenic cases, and in these there was a trend toward lower mean concentration when these subjects were compared with controls. Implications for a biochemical theory of schizophrenia are discussed. (23 references)—Author abstract, modified.

4549. Casper, R.; Garver, D.L.; Dekirmenjian, H.; Chang, S.; and Davis, J.M. (Illinois State Psychiatric Institute, 1601 West Taylor St., Chicago, IL 60612) Phenothiazine levels in plasma and red blood cells: Their relationship to clinical improvement in schizophrenia. Archives of General Psychiatry, 37(3):301–305, 1980.

The relationship between steady-state plasma and red blood cell (RBC) concentrations of the phenothiazine derivative, butaperazine maleate, and the therapeutic response in 24 hospitalized schizophrenics who received constant maintenance doses of butaperazine during the first 2 weeks of treatment was investigated. Butaperazine concentrations in RBCs correlated significantly with clinical improvement in an inverted U-shaped pattern, whereas plasma levels were not significantly related to clinical response. Both plasma levels and RBC levels showed large interpatient variations. The level of RBC bound drug may be a better peripheral correlate of drug levels in the brain than are drug levels in plasma. Thus, monitoring drug levels in RBCs may have an advantage over measuring levels in plasma. These findings, however, may not generalize to other antipsychotic agents. (16 references)—Author abstract, modified.

4550. Costall, B., and Naylor, R.J. (Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, BD7 1DP, England) The relationship between extrapyramidal and mesolimbic GABA and acetylcholine in the mediation of neuroleptic activity. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 450–453.

Research on the role of GABA and acetylcholine in schizophrenic symptomatology is reviewed, and evidence is presented on the relationship between extrapyramidal and mesolimbic GABA and acetylcholine in the mediation of neuroleptic activity. Recent animal studies indicate a cholinergic involvement in neuroleptic actions, but a more complex role is indicated for GABA. The results suggest that GABA mechanisms apparently facilitate or inhibit dopamine-dependent behaviors and may thus exert complex effects on dopamine blockade by neuroleptics. It is concluded that GABA agonists of potential value in neurology and schizophrenia should possess more specific extrapyramidal and mesolimbic effects than do presently available agents. (34 references)

4551. DeFeudis, F.V. (Centre de Neurochimie du C.N.R.S., Faculté de Medicine de Strasbourg, F-67085 Strasbourg Cedex, France) Cholinergic and GABA-ergic systems in schizophrenia. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 445–449.

Research on the role of neurotransmitters in schizophrenia is reviewed, with emphasis on cholinergic and GABA-ergic and, to a lesser extent, dopaminergic mechanisms. It is suggested that neuroanatomical pathways likely to be involved in schizophrenia include the reticular activating, mesolimbic, mesocortical, and extrapyramidal systems. Behavioral and biochemical studies on the effects of neuroleptics and other drugs have revealed relationships among the neurotransmitters. The interference of neuroleptics with dopaminergic mechanisms and the possible role of the drugs in altering dopamine/acetylcholine balance have been demonstrated. The studies have also revealed the likelihood that GABA-like agents possess antipsychotic activity and have shown the possible role of the environment (e.g isolation) in onset of the disease. (40 references)—Author abstract, modified.

4552. Deniker, P.; Loo, H.; Zarifian, E.; Cuche, H.; Benyacoub, K.; Escande, C.; Bousquet, B.; and Dreux, C. (Hôpital Sainte-Anne, Faculté Paris-Cochin, 1, rue Cabanis, F-75014 Paris, France) Measurement of the plasmatic level of free- and protein-bound tryptophan in mental pathology. Neuropsychobiology, 7(3):132–139, 1980.

The plasma levels of free- and protein-bound tryptophan and the free-total tryptophan ratio were measured via an automatic spectrofluorimetric method in 19 normal subjects and in 47 schizophrenic or manic-depressive patients. The only significant difference in the free-total tryptophan ratio was reported in untreated paranoid schizophrenics and in anxiety cases. A dual nosological and symptomatical approach was adopted in the course of attempted correlation with biological data to emphasize the possible role of symptomatic elements common to different diagnoses. It is noted that the elevated free-total tryptophan ratio observed in paranoid schizophrenics returned to normal during treatment, and that this change was paralleled by clinical improvement. The relationship between tryptophan levels and clinical state is discussed in relation to delusive mania, paranoid schizophrenia, and melancholia. (29 references)—Author abstract, modified.

4553. Dotti, A.; Lauro, R.; Bersani, G.; Camagna, A.; and Spallone, L. (Istituto di Clinica

Psichiatrica I, Universita di Roma, Rome, Italy) Study of prolactin variations in psychiatric patients treated with fluphenazine decanoate. Rivista di Psichiatria, 14(3):176–184, 1979.

The utilization of prolactin variations, subsequent to the administration of fluphenazine decanoate, was studied. Twenty patients diagnosed as schizophrenic, who were previously treated with neuroleptics, were administered 25 mg of fluphenazine decanoate every 5 days for a duration of 32 days. The prolactin variations were measured every 20 days for the same time period. Results indicate that prolactin increase was present in all patients administered fluphenazine decanoate, although there was a great variation among patients in the prolactin response to the neuroleptic. It is suggested that a tolerance to the neuroleptic drug was developed in the hypothalamus and hypophyseal axis. (17 references)—Journal abstract, modified.

4554. Freed, W.J.; Kleinman, J.E.; Karson, C.N.; Potkin, S.G.; Murphy, D.L.; and Wyatt, R.J. (Saint Elizabeths Hospital, Laboratory of Clinical Psychopharmacology, Washington, DC 20032) Eye-blink rates and platelet monoamine oxidase activity in chronic schizophrenic patients. Biological Psychiatry, 15(2):329–332, 1980.

Eyeblink rates and platelet monoamine oxidase activity were examined in 30 chronic schizophrenic patients and a group of normal controls. The only group which differed significantly from the control group was a group with schizoaffective illness. Blink rates were significantly elevated in this group. Blinking rates were not altered by conventional neuroleptics, lithium, or benzodiazepines. Platelet MAO activity had previously been determined for 17 of the patients; these MAO values were found to be inversely correlated with eyeblink rates. Results suggest a correlation between platelet MAO activity and central dopaminergic activity as reflected by eyeblink rates. (12 references)

4555. Frohman, C.E. (Lafayette Clinic, Detroit, MI 48233) A tripeptide for control of schizophrenia symptoms. In: Obiols, J.; Bailus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 402–405.

The safety of a tripeptide, threonylvalylleucine, as a treatment for schizophrenia was investigated, and the results on its biological activity are reported. Experiments with rats and beagles injected with a derivative, *N*-acetyl-threonylvalylleucine, were conducted. The results showed a powerful effect on cortical hormones, possibly as a result of a preliminary effect of ACTH, and it is suggested that *N*-acetylthreonylleucine is a hypothalamic polypeptide which inhibits the release of ACTH by the pituitary. An increase in MAO activity was noted, which may have implications for the effective treatment of schizophrenia. (9 references)

4556. Gale, K. (Department of Pharmacology, Georgetown University Schools of Medicine and Dentistry, 3900 Reservoir Road, Washington, DC 20007) Chronic blockade of dopamine receptors by antischizophrenic drugs enhances GABA binding in substantia nigra. Nature, 283(5747): 569–570, 1980.

The effects of chlorpromazine and haloperidol on specific GABA binding in the substantia nigra and striatum of rats were investigated and compared with those of clozapine—an antischizophrenic drug with an atypical biochemical and clinical profile. Data support the hypothesis that chronic blockade of dopamine receptors by classical antischizophrenic drugs enhances GABA binding in the substantia nigra. This effect may be related to the extrapyramidal side effects associated with classical antischizophrenic drug treatment. (40 references)—Author abstract, modified.

4557. Gattaz, W.F., and Beckmann, H. (Zentralinstitut für Seelische Gesundheit, D-6800 Mannheim 1, Germany) HLA antigens and schizophrenia. Lancet, 8159:98–99, 1980.

Results of a study of human leukocyte antigens in 100 schizophrenics and 472 normal controls are reported. HLA A, B, and C loci were typed and antigen frequencies were analyzed. The frequency of HLA B-27 was increased in the patient group as a whole in the subgroups of paranoid patients, chronic schizophrenics, patients with poor prognosis, and those with onset before 20 years old. However, after correction for number of antigens tested, findings were significant only for chronic schizophrenia and those with poor prognosis. Findings support the hypothesis that schizophrenia designates a group of genetically heterogeneous diseases. Possible associations between arthropathy and schizophrenia are also discussed. (6 references)

4558. Giller, E.L., Jr.; Bierer, L.; Rubinow, D.; and Docherty, J.P. (West Haven Veterans Administration Medical Center, West Spring St., West Haven, CT 06516) Platelet MAO V_{max} and K_m in chronic schizophrenic subjects. American Journal of Psychiatry, 137(1):97–98, 1980.

The V_{max} and K_m of platelet monoamine oxidase (MAO) of chronic schizophrenic patients and controls were studied and compared by enzyme assay. The results indicate a lower mean K_m and mean V_{max} in the platelet MAO of chronic schizophrenics than of the controls. It is suggested that the mechanism underlying the decrease still remains uncertain. (10 references)

4559. Giret, M.; Launay, J.M.; Dreux, C.; Zarifian, E.; Benyacoub, K.; and Loo, H. (Hôpital Saint-Louis, Laboratoire de Chimie, F-75475 Paris Cedex 10, France) Modifications of biochemical parameters in blood platelets of schizophrenic and depressive patients. Neuropsychobiology, 6(5):290–296, 1980.

The blood platelet is described as a model of the serotoninergic neuron, and various blood platelet parameters of depressed and schizophrenic patients were measured. Serotonin uptake was found abnormal for all schizophrenics and lowered for depressive patients. Uptake of mepacrine, a marker of serotonin passive diffusion, was diminished for manic patients. MAO and glutathione peroxidase activities were modified, essentially for paranoid schizophrenics, and some alterations of the platelet hydroxyindole level were noticed. Treatment with neuroleptics or antidepressants caused biological parameters to return to normal values. Results are discussed in relation to clinical data and a hypothesis concerning biological functioning of paranoid schizophrenics. (40 references)—Author abstract, modified.

4560. Gjessing, L.R. (Central Laboratory, Dikemark Hospital, N-1385 Solberg, Norway) The switch mechanism in periodic catatonia and manic-depressive disorder. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 307–316.

Research on sudden switches which occur in behavior, in the autonomic nervous system, and in the catecholamine metabolism during the transition from normal interval into catatonic or mania is reviewed. Both the manic and catatonic episodes appear superimposed on the basic depressive or schizophrenic illness and can be counteracted or suppressed by psychotropic drugs which interfere with catecholamine metabolism or their receptor sites. The involvement of the catecholamines may, however, be secondary to primary defects in the hypothalamus. Observations of strict periodicity in periodic catatonia indicates that an accumulation of active metabolites (possibly peptides) may be produced centrally during the interval, may trigger the switch mechanism, and may be inactivated at the end of the active psychotic state. Research on periodic catatonia suggests that both the basic schizophrenic disease and the periodic manifestation are compensated by thyroxine treatment. (8 references)—Author abstract, modified.

4561. Gold, P.; DeFraites, E.; and Zis, A.P. (NIMH, Clinical Psychobiology Branch, Bethesda, MD 20205) The LH response to dopamine infusion: Possible marker for a central dopaminergic function in psychiatric patients. Psychopharmacology Bulletin, 16(2):36–38, 1980.

Luteinizing hormone (LH) and prolactin (PRL) responses to a sustained intravenous infusion of dopamine (DA) in control subjects and drug-free patients with either schizophrenia or major affective illness are described, and the utility of the LH response to dopamine infusion as a marker of central dopaminergic function in psychiatric patients is discussed. The finding that LH responses in both schizophrenic and affectively ill subjects differ from those of normal subjects is compatible with data in experimental animals, which suggest that dopaminergic regulation of LH occurs only within the central nervous system (CNS) via inhibition of hypothalamic luteinizing hormone-releasing hormone, while dopaminergic regulation of PRL secretion occurs both within the CNS and outside at the pituitary level. (9 references)

4562. Golden, C.J.; Moses, J.A., Jr.; Zelazowski, R.; Graber, B.; Zatz, L.M.; Horvath, T.B.; and Berger, P.A. (Department of Medical Psychology, Nebraska Psychiatric Institute, 602 South 45th Street, Omaha, NE 68105) Cerebral ventricular size and neuro-

psychological impairment in young chronic schizophrenics: Measurement by the Standardized Luria-Nebraska Neuropsychological Battery. Archives of General Psychiatry, 37(6):619–623, 1980.

The relationship between size of cerebral ventricles in chronic schizophrenics and performance on the Standardized Luria-Nebraska Neuropsychological Battery (LNNB) was investigated. Ventricular size was determined using a planimeter to measure the size of the lateral ventricles and the ventricular body, if present, on the computerized tomographic (CT) scan image that showed the largest lateral ventricles. Eight of the 14 scales of the LNNB correlated significantly at the .05 level with the ventricular brain ratio (VBR) in a sample of 42 chronic schizophrenics with an average age of 32.3 years. Overall, there was a multiple correlation of .72 between VBR and LNNB scores. The overall VBR for the schizophrenics was significantly above that found in normal populations. Changes in the size of the ventricles in schizophrenics appear to have significant correlates with measures of neuropsychological performance. (32 references)—Author abstract.

4563. Itil, T.M. (Division of Biological Psychiatry, Department of Psychiatry, New York Medical College, New York, NY 10016) Computer analyzed EEG findings in adult schizophrenics, psychotic children and "high risk" children for schizophrenia. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. B. Amsterdam: Elsevier/North Holland, 1979. pp. 1295–1305.

Results of computer analyzed electroencephalogram (CEEG) findings in adult schizophrenics, psychotic children, and high-risk children for schizophrenia are reviewed. They indicate that: (1) adult schizophrenics have an excessive fast activity, along with some slow waves and a lack of alpha activity; (2) excessive fast activity and lack of alpha waves occur in the CEEGs of psychotic children and in children whose parents (particularly the mother) are schizophrenic; (3) findings of schizophrenia resemble those seen after ingestion of hallucinogenic compounds by normals; and (4) the effects of neuroleptics (major tranquilizers) on CEEG are almost diametrically opposite to those seen in schizophrenia. (27 references)—Author abstract, modified.

4564. Johnstone, E.C.; Crow, T.J.; and Cotes, P.M. (Division of Psychiatry, Clinical Research Centre, Watford Rd., Harrow, HA1 3UJ, Middlesex, England) Hormone levels in acute schizophrenia with and without neuroleptic medication. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 476–481.

Anterior pituitary hormones and testosterone were measured before and at weekly intervals during a 4-week trial of α-flupenthixol, β-flupenthixol, and placebo in patients with acute schizophrenia. Prolactin levels rose substantially in patients receiving α-flupenthixol, but there were few changes in the other two groups. Levels of the other hormones did not change significantly over the 4 weeks. Of the hormones studied, changes in serum prolactin were the only ones significantly related to the antipsychotic effect. There was a temporal dissociation between rise in prolactin level and antipsychotic effect. The implications of these results for the role of dopamine receptor blockade and the central monoaminergic systems in the antipsychotic effect are discussed. (9 references)—Author abstract, modified.

4565. Kato, N.; Miyamoto, Y.; Imai, H.; Arima, S.; and Kimura, H. (Department of Neuropsychiatry, Kyoto Prefectural University of Medicine, Kyoto, Japan) Are there biological deficits in schizophrenia? In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 424–433.

The possibility of biological deficits in schizophrenia was investigated by studying the activity of dopamine-β-hydroxylase (DBH) and creatine phosphokinase (CPK) in serum and of cyclic AMP in plasma. The findings indicate: (1) a wide variation in serum DBH level, although levels were generally lower than those of controls; (2) increased serum CPK activity; and (3) increased levels of plasma cyclic AMP, accompanied by increased heartrate. Implications of the findings for biochemical studies of inborn error in metabolism among schizophrenics and for the dopamine hypothesis of schizophrenia are discussed. It is concluded that disturbances of the reciprocal neuronal circuit between the dopamine innervating cortical area and mesencephalic dopamine cell bodies relate to the etiology of the disorder. (8 references)

4566. Kemali, D.; Vacca, L.; Marciano, F.; Celani, T.; Nolfe, G.; and Iorio, G. (Clinica Psichiatrica I.a Facolta di Medicina e Chirugia, Piazza Miraglia 2, Naples, Italy) Computerized EEG in schizophrenics. Neuropsychobiology, 6(5):260–267, 1980.

A computerized electroencephalographic (EEG) investigation of 20 psychiatric patients without pharmacologic therapy and a homogeneous control group of 19 healthy subjects is described. Computerized spectral analyses of the main EEG frequency bands are presented. The spectra were determined by geometrical descriptors: relative activity, barycentric frequency, and barycentric radius. In the EEG profile, significant differences between subgroups were also found. The geometrical descriptors applied in the EEG analysis were suggested as a useful method in the description of the basic characteristics of the main EEG frequency bands. (23 references)—Author abstract, modified.

4567. Kitamura, T.; Mizuguchi, R.; and Hara, T. (Department of Psychiatry, University of Birmingham, Birmingham, England) The change of blood prolactin level due to the withdrawal of maintenance neuroleptics. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 711–713.

Thirteen chronically institutionalized male psychiatric patients—12 of whom were schizophrenic—were studied for change of blood prolactin (PRL) level as a result of withdrawal of maintenance neuroleptics. Blood levels of PRL, luteinizing hormone, follicle stimulating hormone, growth hormone (GH), thyrotropin, serotonin, immunoreactive insulin, glucose, free fatty acids, and triglyceride were estimated, and a 50 g glucose tolerance test was done before and after the drug holiday. No changes occurred after withdrawal except with PRL and GH. PRL was normal before withdrawal and fell to the lower limit of the normal range after withdrawal. More GH was released in the glucose tolerance test after withdrawal. The concept of hypersensitivity of the CNS, particularly tuberoinfundibular dopaminergic system, is consistent with the findings. (6 references)—Author abstract, modified.

4568. Kleine, T.O., and Kroh, U. (Klinisch-chemisches Labor, Universitäts-Nervenklinik, Marburg/Lahn, West Germany) Effect of fluphenazine on the circadian excretion of cyclic nucleotides and electrolytes in the urine of chronic schizophrenics. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 317–322.

The circadian excretion of cyclic AMP and cyclic GMP, together with electrolytes, was examined in the urine of five healthy normal men and two chronic male schizophrenics to assess the effect of fluphenazine on these parameters. Excretion was altered in the urine of the two patients, and these results suggest disturbances in the interior body time of schizophrenics. Fluphenazine further affected the circadian excretion pattern of cyclic AMP and cyclic GMP in the schizophrenics and, to a smaller extent, that of electrolytes. (5 references)—Author abstract, modified.

4569. Kolyaskina, G.I. (Institute of Psychiatry, A.M.S., Moscow, USSR) Antithymic antibodies in schizophrenia. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 418–423.

Serum samples from normals and schizophrenic patients were observed for antithymic antibody activity in an international study of the immunology of schizophrenia. It was found that the average level of blood serum antithymic activity in schizophrenics was much higher than in the group of normal controls. The level of the blood serum antithymic activity depended on the duration of the disease. Also, the maximum frequency of detection of blood serum with high level of antithymic activity occurred when the disease duration was under 5 years. The results suggest the possibility of higher risk for schizophrenia among normals with a high level of this antibody in the blood serum. (2 references)—Author abstract, modified.

4570. Kugler, B.T., and Gruzelier, J.H. (Charing Cross Hospital Medical School, Fulham Palace Rd., London W6 8RF, England) The influence of chlorpromazine and amylobarbitone on the recovery limb of the electrodermal re-

sponse. Psychiatry Research, 2(1):75–84, 1980.

To examine the effects of chlorpromazine and amylobarbitone on the recovery limb of the electrodermal response, 12 healthy normal subjects were administered single oral doses of chlorpromazine, amylobarbitone, and a placebo in a double-blind, latin square design. Skin conductance was recorded bilaterally from bipolar placements of silver/silver chloride cup electrodes. Skin conductance ordering responses were examined to 13 tones of 1000 Hz presented at variable intervals. Results show that chlorpromazine, but not amylobarbitone, influenced the scope of the recovery limb of responses to simple oriented stimuli with no signal significance. Results detract from existing evidence that the slope of the recovery limb of the electrodermal response is an indicator of schizophrenia. (26 references)

4571. Lake, C.R.; Sternberg, D.E.; van Kammen, D.P.; Ballenger, J.C.; Ziegler, M.G.; Post, R.M.; Kopin, I.J.; and Bunney, W.E., Jr. (Department of Psychiatry and Pharmacology, Uniformed Services Medical School, Bethesda, MD 20814) Schizophrenia: Elevated cerebrospinal fluid norepinephrine. Science, 207(4428): 331–333, 1980.

Norepinephrine (NE) concentrations in the cerebrospinal fluid of 35 schizophrenic patients and 29 healthy volunteers were measured. The concentrations of NE were higher in schizophrenic patients, particularly in those with paranoid features, than in normal volunteer subjects of the same age. This observation supports recent reports of elevated concentrations of NE in specific brain areas adjacent to the cerebral ventricles of paranoid schizophrenic patients. It is concluded that overflow of the amine from periventricular regions into the cerebrospinal fluid may reflect abnormally high release or diminished enzymatic destruction of NE in patients with schizophrenia. (16 references)—Author abstract, modified.

4572. Langer, G. (Department of Psychiatry, University of Vienna School of Medicine, Vienna, Austria) The hypothalamic dopaminergic regulation of prolactin: A model for the study of neurohormonal mechanisms in man. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 699–704.

Neuroendocrinological and pharmacological studies of normal young men and schizophrenic patients are reviewed to examine the theory that lactotrophic cells of the pituitary gland may serve as a reliable and valid model for studying neurohormonal (particularly dopaminergic) mechanisms in man. It is reported that: (1) human plasma prolactin (PRL) concentrations may be increased reliably by administration of a neuroleptic (NL) drug; (2) the increase is dose related and highly reproducible within a subject; (3) a small dose of an NL may significantly elevate PRL levels, while a dose well below the regimen given to treat schizophrenics induces maximal PRL response; (4) the relative potencies of seven NLs in releasing PRL in man and in treating acute schizophrenic patients are highly correlated; and (5) the pituitary's lactotrophic cells are the locus of action of NLs in releasing PRL in stalk-sectioned monkeys and in normal men. (15 references)—Author abstract, modified.

4573. Lee, T., and Seeman, P. (Department of Pharmacology, Medical Sciences Bldg., University of Toronto, Toronto, Ontario, Canada M5S 1A8) Elevation of brain neuroleptic/dopamine receptors in schizophrenia. American Journal of Psychiatry, 137(2):191–197, 1980.

To test the dopamine hypothesis of schizophrenia, the specific ^{3}H-neuroleptic/dopamine binding sites in three dopamine-rich regions of 59 post-mortem normal human brains and 50 post-mortem brains from schizophrenic patients using ^{3}H-haloperidol and ^{3}H-spiperone were examined. The binding of 2 *nM* ^{3}H-haloperidol and of 1 *nM* ^{3}H-spiperone was significantly elevated in schizophrenic brains. The brain regions from schizophrenic subjects with no history of being treated with neuroleptic drugs also exhibited significantly higher binding of the ^{3}H-neuroleptics. These results are compatible with the hypothesis that schizophrenia may be associated with an overactivity of postsynaptic dopamine receptors. (55 references)—Author abstract, modified.

4574. Loosen, P.T.; Prange, A.J., Jr.; and Wilson, I.C. (Department of Psychiatry, School of Medicine, University of North Carolina, Raleigh, NC) The TSH response to TRH injection in psychiatric patients: A review. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psy-

chiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 780–784.

Thyrotropin releasing hormone (TRH) was injected in depressed, alcoholic, and schizophrenic patients to study the resulting psychoendocrinological conditions. Thyroid stimulating hormone (TSH) and cortisol were analyzed at baseline, along with the TSH response to TRH and the relationship between the two hormones. TSH blunting was found in some depressed and some alcoholic patients, but not in schizophrenics. The relationship between cortisol and TSH peak response was negative in depressed subjects and normal subjects, and was random in alcoholic patients. Schizophrenics, however, showed a tendency toward a positive relationship between these variables. (28 references)—Author abstract, modified.

4575. Luchins, D.; Torrey, E.F.; Weinberger, D.R.; Zalcman, S.; Delisi, L.; Johnson, A.; Rogentine, N.; and Wyatt, R.J. (St. Elizabeths Hospital, William A. White Bldg., Washington, DC 20032) HLA antigens in schizophrenia: Differences between patients with and without evidence of brain atrophy. British Journal of Psychiatry, 136:243–248, 1980.

The association between specific HLA antigens and schizophrenia was investigated in 130 schizophrenic inpatients using recognized diagnostic criteria and CT scan findings. Among 92 black schizophrenic patients, there was an increase of HLA-A_2, which remained significant even after correcting for the number of antigens studied. When the patients were divided according to the presence or absence of evidence of brain atrophy, there was an increase of A_2 in the black schizophrenic patients without evidence of atrophy. However, there was no significant increase of A_2 in those with evidence of atrophy. Similar trends held for the white population but failed to reach significance. The need for HLA studies on biologically defined groups of schizophrenic patients is stressed. (25 references)—Author abstract, modified.

4576. McGuffin, P. (Maudsley Hospital, Denmark Hill, London SE5, England) The HLA system and schizophrenia in England. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 85–89.

Data on the distribution of HLA antigen frequencies in British schizophrenic patients are discussed, and results are reported from a study of the effects of neuroleptics on a subsample of these subjects. A group of 80 patients were HLA typed for 25 A-series and B-series antigens, and it was concluded that a reported association of HLA A28 is of dubious importance. More promising results were obtained, however, for the relationship between HLA and diagnostic subtypes. Findings on the effect of neuroleptics on 28 of the subjects suggested a susceptibility to drug induced parkinsonism and supported the hypothesis that HLA antigens may influence responsiveness of cell surface receptors to certain ligands—dopamine blocking drugs. (20 references)

4577. McSwigan, J.D. (University of Minnesota, Minneapolis, MN 55455) Effects of dopamine and anti-schizophrenic drugs on enzymatic parameters of adenylate cyclase from rat striatum. Dissertation Abstracts International, 40(9):4556–B, 1980.

The effects of dopamine and anti-schizophrenic drugs on enzymatic parameters of adenylate cyclase from rat brain striatum were investigated. Guanyl nucleotides were found to stimulate the adenylate cyclase. The concentration dependence of guanyl nucleotide activation was investigated using the nonhydrolyzable analog of guanosine triphosphate, guanylylimidodiphosphate. Also, the effect of free Mg^{2+} ion, which has been shown to be a required activator for adenylate cyclase from other tissue, was examined for concentration dependent effects. Results indicate that the major effect of dopamine is on the affinity of dopamine sensitive adenylate cyclase for free Mg^{2+} and guanyl nucleotide. Various possible differences which could account for altered hormonal response between schizophrenics and normals are discussed.—Journal abstract, modified.

4578. Maricq, H.R., and Weinrich, M.C. (Department of Medicine, Medical University of South Carolina, Charleston, SC 29403) Psychophysiological studies in schizophrenic patients selected on the basis of a "genetic marker." Acta Psychiatrica Scandinavica, 61(3):185–208, 1980.

The use of a biological marker—the high plexus visualization score (PVS)—to provide a better psychophysiological separation of schizophrenic and control subjects was investigated. Finger blood flow, skin temperature, and electrodermal recovery rates were studied in 64 male schizophrenics—33 high PVS and 31 low PVS—and 24 male controls. Results indicate that schizophrenics with high PVS had the lowest finger blood flow rates, the lowest skin temperature, and the slowest GSR recovery rates of all groups studied. The largest difference in all three variables was found between high PVS schizophrenics and high PVS controls. It is reported that blood flow rates and skin temperature were higher and electrodermal responses were fewer in patients taking medications than those receiving placebos. (37 references)—Author abstract, modified.

4579. Mathe, A.A.; Sedvall, G.; Wiesel, F.A.; and Nyback, H. (Department of Psychiatry, Mount Sinai School of Medicine, New York, NY 10029) Increased content of immunoreactive prostaglandin E in cerebrospinal fluid of patients with schizophrenia. Lancet, 8158:16–18, 1980.

Immunoreactive prostaglandin E (I-PGE) and thrombaxane B_2 (I-TxB_2) were measured in cerebrospinal fluid from patients with schizophrenia and from control subjects. Schizophrenics had higher I-PGE concentrations than healthy controls, patients classified as neurotics, and patients admitted for neurological investigation. I-TxB_2 concentrations were similar in all four groups. These preliminary results are consistent with the hypothesis that at least in some forms of schizophrenia there may be an alteration of prostaglandin synthesis or metabolism. (13 references)—Author abstract.

4580. Meltzer, H.Y., and Arora, R.C. (Department of Psychiatry, University of Chicago, 950 E. 59th St., Chicago, IL 60637) Skeletal muscle MAO activity in the major psychoses. Archives of General Psychiatry, 37(3):333–339, 1980.

Evidence is presented that the skeletal muscle MAO acitivity of schizophrenics and patients with bipolar and unipolar affective psychoses is lower than that of normal controls. Both platelet and plasma MAO activities are significantly lower in schizophrenics and patients with undiagnosed psychoses than in controls. The decrease in skeletal muscle MAO activity in various psychotic patients is consistent with previous suggestions based on platelet studies that low MAO activity may be a nonspecific factor contributing to development of different forms of psychopathology. Since total skeletal muscle MAO activity is the largest source of MAO in the body, it is possible that the decrease in muscle MAO activity may lead to excessive quantities of biogenic amines that could adversely affect neural activity. (77 references)— Author abstract, modified.

4581. Mendlewicz, J., and Linkowski, P. (Department of Psychiatry, Erasme Hospital, Free University of Brussels, Brussels 1070, Belgium) HLA antigens and schizophrenia. Lancet, 8171:765, 1980

The relationship between HLA antigen frequencies and schizophrenia was studied in 64 chronic schizophrenics with poor prognosis and 113 controls. The results indicate an excess BW16 and a deficit in A1 and B7 in schizophrenic patients, but no association with B27 was found. Methodological reasons for these results are considered. (3 references)

4582. Naeser, M.A.; Levine, H.L.; Benson, F.; Stuss, D.T.; and Weir, W.S. (Medical Center (116-B), 150 S. Huntington Avenue, Boston, MA 02130) Frontal leukotomy size and hemispheric asymmetries on computerized tomographic scans of schizophrenics with variable recovery. Archives of Neurology, 38(1): 30–37, 1981.

The computerized tomographic (CT) scans of 17 schizophrenic men who had had bilateral prefrontal leukotomy performed 25 years earlier were examined to determine the relationship among leukotomy sites, size, hemispheric asymmetries, and recovery. Six cases of good recovery (GR), five of moderate recovery (MR), and six of no recovery (NR) were studied. Sixteen of the 17 patients were right-handed. Results showed that the GR cases had significantly larger lesions in the low orbitofrontal region (especially on the left) than did the other MR and NR cases. Also, five of six of the GR cases had significantly greater lesion size asymmetry in the low orbitofrontal region than did the other MR and NR cases. There was no consistent asymmetry of lesion size (larger right or left) that was associated with recovery. Significant differences were observed in the hemispheric asymmetries of the right-handed schizophrenics versus normal subjects. Additional findings are considered, and additional observation of longstanding leukotomy sites on CT scans in schizophrenia cases is recommended. (45 references)—Author abstract, modified.

4583. Parisi, H.A.; Lanara, E.C.; and Triantaphyllidis, C.D. (Laboratory of General Biology, University of Thessaloniki, Thessaloniki, Greece) Protein and enzyme polymorphisms in affective disorders in northern Greece. Human Heredity, 30(3):181–184, 1980.

The phenotype and gene frequencies of hemoglobins, haptoglobins, albumins, and eight polymorphic enzyme systems were electrophoretically determined in 225 patients with affective disorders from northern Greece in an attempt to explore their genetic structure. Of the 225 patients, 95 were suffering from schizophrenia. In five polymorphic systems studied, no significant differences were found between the gene frequencies of the total sample and the normal controls and between the schizophrenic group and either the total sample or the controls. (10 references)—Author abstract, modified.

4584. Rauscher, F.P.; Nasrallah, H.A.; and Wyatt, R.J. (St. Elizabeths Hospital, William A. White Bldg., Washington, DC 20032) Cutaneous histamine response in schizophrenia. Journal of Clinical Psychiatry, 41(2):44–51, 1980.

Twelve studies over the past 50 years were reviewed in which a diminished cutaneous response to intradermal histamine in schizophrenics had been reported. This literature is compared with an investigation in which both the wheal and flare response to intradermal histamine is examined in chronic schizophrenic patients, their parents, and a healthy control group. Histamine insensitivity could not be demonstrated in unmedicated patients, although a diminished wheal and flare response occurred during neuroleptic treatment. A cutaneous histamine insensitivity does not appear to be a common phenomenon among chronic schizophrenic patients. (42 references)—Author abstract, modified.

4585. Rimon, R.; Liira, J.; Kampman, R.; and Hyyppa, M. (Department of Psychiatry, University of Helsinki, Helsinki, Finland) Prolactin levels in cerebrospinal fluid of patients with chronic schizophrenia. Neuropsychobiology, 7(2):87–93, 1981.

Baseline concentrations of prolactin (PRL) were determined in the cerebrospinal fluid (CSF) of 28 lobotomized and 28 nonlobotomized patients with chronic schizophrenia. The mean PRL level of the female patients was significantly higher than that of the male patients. In addition, nonlobotomized patients had significantly higher concentrations of CSF PRL than patients of the lobotomized group. However, patients belonging to the latter group exhibited significantly more central as well as cortical brain atrophy than the patients who had not received psychosurgery. The significance of CSF PRL as an index of central dopamine metabolism is discussed. (50 references)—Author abstract, modified.

4586. Roth, W.T.; Horvath, T.B.; Pfefferbaum, A.; and Kopell, B.S. (Veterans Administration Medical Center, Laboratory of Clinical Psychopharmacology and Psychophysiology, Palo Alto, CA 94304) Event-related potentials in schizophrenics. Electroencephalography and Clinical Neurophysiology, 48(2):127–139, 1980.

The event-related potential (ERP) components elicited by the tone interval, reaction time, and noise/tone paradigms were compared in 15 schizophrenics and 15 age-matched controls. The sensitivity of some of the ERP components in distinguishing schizophrenics from controls depended on the conditions under which the component was elicited. N1 amplitude was smaller in schizophrenics than in controls after long interstimulus intervals. P2 amplitude was smaller in the schizophrenics only at high stimulus intensities. P2 latency was generally shorter in schizophrenics, but not when interstimulus intervals were varied. P3 amplitude was much smaller in schizophrenics than in controls. Loud stimuli elicited blink reflexes that coincided with N1, but these reflexes did not vary by group. The amplitude of the slow wave following targets and the sustained potential associated with prolonged auditory stimuli did not differ between schizophrenics and normals. (47 references)

4587. Rotrosen, J., and Gershon, S. (Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016) Growth hormone, prostaglandins, and receptor sensitivity in schizophrenia. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol.

A. Amsterdam: Elsevier/North Holland, 1979. pp. 123–127.

A series of studies of growth hormone (GH), prostaglandins, and receptor sensitivity in schizophrenia are described. As an independent measure of receptor function, the accumulation of ^{3}H-cyclic AMP in pulse labeled platelets incubated with prostaglandin E_1 (PGE$_1$) were assessed. PGE$_1$ stimulated ^{3}H-cyclic AMP accumulation in platelets from schizophrenics was significantly reduced compared to this same response in platelets from control subjects. Reduced responses were seen in both acute and chronic schizophrenics, and in schizophrenics both on and off neuroleptic drugs. It is noted that identification of a prostaglandin deficiency in schizophrenia could provide a basis for development of rational and novel pharmacotherapies such as treatment with prostaglandin precursors, substances thought to enhance prostaglandin synthesis, or substances that mimic the effects of prostaglandins. (32 references)

4588. Rudin, D.O. (Department of Molecular Biology, Eastern Pennsylvania Psychiatric Institute, Philadelphia, PA 19129) The choroid plexus and system disease in mental illness. I. A new brain attack mechanism via the second blood-brain barrier. Biological Psychiatry, 15(4):517–539, 1980.

A theory is evolved based on the role of the choroid plexus and system disease in mental illness. Schizophrenia and certain idiopathic neuroses and retardations may be caused by polygenic sensitization to exogenous peptide antigens or viruses causing a covert immune complex basal lamina disease of the choroid plexus. This organ has the general structure and disease susceptibility of many other transport organs but acts as a second blood-brain barrier. The actual cytoarchitecture of the barriers to the brain are examined. The exocrine, endocrine, and transport organs are described. Because of the shared entrapping tissue membrane configuration, all are vulnerable to immune complex disease. Thus, schizophrenia and other diseases are viewed as variants of combined transport dysfunction. (49 references)—Author abstract, modified.

4589. Shagass, C. (Department of Psychiatry, Temple University, Philadelphia, PA 19122) New findings in brain potential investigations of schizophrenia. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds., Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 454–459.

Recent research concerning event-related potential (ERP) investigations of schizophrenia are reviewed. Results indicate that the topography of some ERPs is deviant in schizophrenia and that there may be left hemisphere involvement. Discrimination of ERP measurements between subtypes of schizophrenia may be of particular value. However, few differences seem to be specific for schizophrenia. When other types of psychiatric patients have been studied in addition to schizophrenics, the measures discriminating schizophrenics often discriminated other patients from normals. (13 references)—Author abstract, modified.

4590. Shagass, C.; Roemer, R.A.; Straumanis, J.J.; and Amadeo, M. (Department of Psychiatry, Temple University, Philadelphia, PA 19122) Evoked potential evidence of lateralized hemispheric dysfunction in schizophrenia. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. B. Amsterdam: Elsevier/North Holland, 1979. pp. 1335–1339.

Evoked potentials (EPs) elicited by visual (VEP), auditory (AEP), and right and left median nerve (somatosensory, SEP) stimuli were recorded from 15 electrodes to determine whether differences in hemispheric function can be demonstrated in schizophrenia. Measures of hemispheric lateralization revealed group differences in degree of asymmetry in VEP waveshape variability. Left VEP variability values for latent schizophrenics were greater than normal and less than those of overt schizophrenics. AEP variability also was relatively greater in the left than in the right hemisphere in schizophrenics. The asymmetry in VEP stability values was abolished by antipsychotic drugs. The findings suggest that schizophrenia is associated with relative left hemisphere dysfunction (instability). (8 references)— Author abstract, modified.

4591. Siris, S.G.; Siris, E.S.; van Kammen, D.P.; Docherty, J.P.; Alexander, P.E.; and Bunney, W.E., Jr. (Department of Psychiatry, Mount Sinai Hospital, One Gustave Levy Pl., New York, NY 10024) Effects of dopamine blockade on gonadotropins and testosterone in men. American Journal of Psychiatry, 137(2):211–215, 1980.

The effects of neuroleptic medication on the hypothalamic pituitary gonadal axis in schizophrenic males were investigated. Plasma luteinizing hormone (LH), prolactin, and testosterone were initially normal in nine acutely psychotic males with schizophrenia or schizoaffective disorder, while follicle stimulating hormone (FSH) was normal in eight of the nine subjects. Following treatment with pimozide, a dopamine receptor blocker, significant declines occurred in FSH and LH although levels remained within normal limits. Prolactin rose significantly, but testosterone did not change. These reductions are consistent with the hypotheses that dopamine and/or prolactin are involved in gonadotropin secretion. The maintenance of normal levels of gonadotropins and testosterone, however, suggests that these subjects possess relatively normal hypothalamic pituitary gonadal axis function before and during neuroleptic treatment. (26 references)—Author abstract, modified.

4592. Stefanis, C.N.; Lykouras, E.; Garelis, E.; and Varsou, E. (Department of Psychiatry, Athens Medical School, Eginition Hospital, Athens, Greece) Cyclic AMP in psychoses and the effect of drugs. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 149–154.

Plasma cAMP in manic-depressive and schizophrenic patients was studied before and after neuroleptic drug treatment. The results are reviewed in correlation with currently held views on the biological mechanisms underlying this type of psychosis. Findings from preliminary investigations on diurnal and longitudinal variation of cAMP, as well as on the effect of physical activity on this nucleotide, are also reported. Results indicate that plasma cAMP concentrations are not significantly altered in the course of schizophrenic illness, and cAMP levels in manic-depressive patients were found to be more highly correlated with the mood rating than with the physical activity scoring. Additional factors that contribute to or influence the degree of physical activity are mentioned. (27 references)—Author abstract, modified.

4593. Stevens, J.R. (University of Oregon Health Sciences Center, Portland, OR 97201) Dopamine and schizophrenia. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 246–251.

Research on central dopamine regulation as a potential key to the pathophysiology of schizophrenia is reviewed. Such research has focused on the anatomy of the cerebral dopamine systems and suggests the specific role of dopamine turnover in mesolimbic and neostriatal systems. Experimental studies of GABA blockade and kindling in the mesolimbic system have used animal models of psychosis. Clinical studies have focused on the striatofugal systems to assess evidence that temporal lobe epilepsy and schizophrenia may reflect a disturbance of different levels of the limbic system. Oculomotor disturbances in schizophrenics have also been examined in support of the view that dopamine potentiation in the mesolimbic system decreases the threshold elicitation of ocular searching automatisms in response to external stimuli. (20 references)

4594. Sullivan, J.L.; Coffey, C.E.; Basuk, B.; Cavenar, J.O.; Maltbie, A.A.; and Zung, W.W.K. (Department of Psychiatry, Veterans Administration Medical Center, 508 Fulton Street, Durham, NC 27705) Urinary tryptamine excretion in chronic schizophrenics with low platelet MAO activity. Biological Psychiatry, 15(1):113–120, 1980.

Urinary tryptamine excretion was examined in chronic schizophrenics with low platelet MAO activity, in chronic schizophrenics with normal platelet MAO activity, and age-matched and sex-matched control subjects. Reduced platelet MAO activity has been reported previously as a biochemical marker for a subgroup of psychiatric patients, including some chronic schizophrenics. The increased urinary tryptamine excretion observed in chronic schizophrenics with low platelet MAO activity may reflect a pathophysiologic mechanism associated with low MAO activity. (24 references)—Author abstract, modified.

4595. Torrey, E.F. (NIMH Saint Elizabeths Hospital, Arthur P. Noyes Division, Washington, DC 20032) Neurological abnormalities in schizophrenic patients. Biological Psychiatry, 15(3):381–388, 1980.

Neurological abnormalities were studied in schizophrenic patients using a test for graphethesia and the face/hand test. Eight percent of the acute/subacute group versus 49 percent of the subchronic/chronic group were abnormal. Abnormalities tended to be more pronounced on the right hand, consistent with other recent lateralization findings suggesting that schizophrenia involves the left cerebral hemisphere. Patients with positive findings had been psychotic longer and were more likely to have been referred to a psychiatrist prior to age 17. The possibility of drug-related symptoms was a confounding issue. (33 references)—Author abstract, modified.

4596. Trimble, M.R., and Meldrum, B.S. (National Hospital for Nervous Diseases, Queen Square, London, England) Monoamines, epilepsy and schizophrenia. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 470–475.

The relationship between the ability of antidepressant drugs to alter monoaminergic transmission and their effect on the seizure threshold in epilepsy was investigated using an animal model. Findings obtained with chlorimipramine, imipramine, maprotiline, and nomifensine indicated a spectrum of the convulsant potential and demonstrated a relationship between seizure threshold and dopamine activity, such that dopamine agonists raise seizure threshold and are antiepileptic, and dopamine antagonists lower the threshold and are epileptogenic. The possibility that dopamine systems are not only related to modulation of the seizure threshold, but also to the psychotic threshold in schizophrenia was then examined. Empirical confirmation of the view would demonstrate a relationship between epilepsy and schizophrenia. (27 references)

4597. Tune, L.E.; Creese, I.; Coyle, J.T.; Pearlson, G.; and Snyder, S.H. (Johns Hopkins University School of Medicine, Baltimore, MD 21205) Low neuroleptic serum levels in patients receiving fluphenazine decanoate. American Journal of Psychiatry, 137(1):80–82, 1980.

Serum levels of fluphenazine in nine schizophrenic patients were monitored following injections of fluphenazine decanoate ranging from 10 to 75 mg. Levels were detected by a radioreceptor assay based on the ability of the rat caudate membranes. Serum levels of fluphenazine were quite stable over a 2- to 3-week period following single intramuscular injections of the decanoate and correlated with injected dose. Following decanoate treatment, serum levels of fluphenazine were substantially lower than levels observed for most other neuroleptics administered orally. Questions as to how fluphenazine decanoate can exert therapeutic actions are considered. (18 references)—Author abstract.

4598. Tune, L.E.; Creese, I.; DePaulo, J.R.; Slavney, P.R.; Coyle, J.T.; and Snyder, S.H. (Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205) Clinical state and serum neuroleptic levels measured by radioreceptor assay in schizophrenia. American Journal of Psychiatry, 137(2): 187–190, 1980.

Serum neuroleptic levels were determined via radioreceptor assay in 30 schizophrenic patients receiving haloperidol, fluphenazine, chlorpromazine, molindone, thiothixene, or trifluoperazine. Neuroleptic levels were significantly correlated with clinical state, monitored by an abbreviated version of the Present State Examination. Poor therapeutic responses were associated with serum levels under 50 ng/ml chlorpromazine equivalents. There was no correlation between neuroleptic dosage and PSE score or between neuroleptic dose and serum neuroleptic levels. (21 references)—Author abstract, modified.

4599. Ucha-Udabe, R. (No address given) Schizophrenia and the prostaglandins. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 740–745.

The cause and effect relationship between schizophrenia and the prostaglandins is discussed. All psychoactive drugs, including those administered to schizophrenic patients, stimulate secretion of prolactin, which itself stimulates prostaglandin synthesis. Schizophrenics are more resistant to pain and inflammation—a phenomenon which has been linked to the prostaglandins. Moreover, high doses of anti-inflammatory drugs cause schizophrenia in many cases. Implications for treatment and for further research are discussed.

4600. Ulrich, G. (Abt. fur Psychophysiologie der Freie Universitat, Nussbaumallee 32-38, D-1000 Berlin 19, West Germany) Problems

of functional lateralization in psychiatric research. Fortschritte der Neurologie-Psychiatrie und ihrer Grenzgebiete, 47(8):418–430, 1979.

Investigations by Flor-Henry of patients with endogenomorphic epileptic psychoses are discussed. The theory claims that there is a critical involvement of the left hemispheric temporolimbic system in schizophrenia and of the right temporolimbic system in affective psychoses. The interpretation of findings of Gruzelier et al. of asymmetrically altered electrodermal activity in functional psychoses is discussed, particularly with reference to the untenable assumption of a central control of sweat gland activity via uncrossed descending limbicofugal fibers. In addition, an attempt is made to interpret these obviously state-dependent electrodermal findings as a dispositional variable, and to infer from this a genetically determined dysfunction in one or the other hemisphere. Some of the findings which seem to be diametrically opposed to Flor-Henry's theory, as well as experimental results of Dimond and Beaumont suggesting a disturbed functional coordination of both hemispheres in schizophrenia, are summarized. A systems theory oriented conceptual framework is outlined which should allow alignment of lateralization findings in schizophrenia and affective psychoses, and which assigns a central position to the constructs of vigilance and maturation and permits an interweaving of the dynamics of structure and the developmental biological points of view. (86 references)—Journal abstract, modified.

4601. van Kammen, D.P.; Docherty, J.P.; and Marder, S.R. (Biological Psychiatry Branch, NIMH, Bldg 10, Rm 4N214, 9000 Rockville Pike, Bethesda, MD 20205) Lack of behavioral supersensitivity to *d*-amphetamine after pimozide withdrawal. Archives of General Psychiatry, 37(3):287–290, 1980.

The postulated relationship between psychotic decompensation as observed after *d*-amphetamine infusion and the dopamine receptor supersensitivity expected to be present during the neuroleptic withdrawal period was examined in 12 schizophrenic patients. A 20 mg i.v. dose of *d*-amphetamine did not cause a stronger psychotogenic effect. One week after discontinuation of pimozide treatment, the *d*-amphetamine induced change was not significantly different from the response to a similar infusion during the drug-free state. Unexpectedly, the increase in Brief Psychiatric Rating Scale mannerisms (paranoid disturbance cluster score) and posturing item and in the pulse rate response to *d*-amphetamine were decreased. The results question the role of dopamine in *d*-amphetamine effects and suggest postneuroleptic dopamine receptor sensitivity. (41 references) —Author abstract, modified.

4602. Walton, A.H. (No address given) Conjugate lateral eye movement, brain dysfunction and asymmetry of hemispheric function. Dissertation Abstracts International, 40(12):5836–B, 1980.

The relationships among conjugate lateral eye movement (CLEM), brain dysfunction, and asymmetry of hemispheric function were investigated among college students, alcoholics, and schizophrenics. Consistent CLEMs to the right (RMs) and consistent CLEMs to the left (LMs) were hypothesized to indicate a preference for the use of the cerebral hemisphere contralateral to the eye movement in processing information. Tests to reflect left hemisphere activity (Word Definition Test) and right hemisphere activity (Facial Recognition Test) were administered to 91 right-handed subjects. Results indicate that 71 percent of all subjects had CLEMs in a consistent direction. The distributions of LMs, RMs, and mixed among the student and schizophrenic groups were similar to those reported in the literature. However, a significant number of alcoholics were found to be LMs. No significant differences between groups on measures of left and right hemisphere functioning were found.—Journal abstract, modified.

4603. Weinberger, D.R.; Kleinman, J.E.; Luchins, D.J.; Bigelow, L.B.; and Wyatt, R.J. (St. Elizabeths Hospital, William A. White Building, Washington, DC 20032) Cerebellar pathology in schizophrenia: A controlled postmortem study. American Journal of Psychiatry, 137(3):359–361, 1980.

A morphometric study of the anterior cerebellar vermis of 47 human brains in the Yakovlev collection was undertaken. The area of the vermis of 5 of 12 brains of schizophrenic patients was smaller than that of any of 11 brains of control subjects without psychiatric or neurologic disease and of 9 of 10 brains of control subjects with other psychiatric diagnoses. This finding confirms computerized tomography scan observations in live patients and supports the idea that some schizophrenics have structural abnormalities of the cerebellar vermis. (15 references)—Author abstract, modified.

4604. Weinberger, D.R., and Wyatt, R.J. (Adult Psychiatry Branch, Division of Special Mental Health Research, NIMH, Saint Elizabeths Hospital, Washington, DC 20032) Structural brain abnormalities in chronic schizophrenia: Computed tomography findings. In: Baxter, C., ed. Perspectives in Schizophrenia Research. New York: Raven Press, 1980. pp. 29–41.

Computed tomography studies of schizophrenic patients are reviewed, and the four types of abnormalities of brain structures found are discussed. The four types are: (1) enlargement of the cerebral ventricles; (2) dilatation of several fissures on the surface of the brain; (3) apparent atrophy of a portion of the cerebellum; and (4) atypical asymmetries between various aspects of the cerebral hemispheres. The first three of these findings suggests subtle degeneration of brain tissue. The fourth finding has also been associated with various cognitive disorders, such as autism and dyslexia. Approximately two thirds of the chronic schizophrenic patients studied have at least one of these abnormalities. However, many patients have only one abnormality, and some have none. The findings support the notion that schizophrenia is not a unitary disease entity, but a heterogeneous collection of abnormalities of higher brain function that may result from various causes. (45 references)

4605. Whitaker, P.M.; Crow, T.J.; and Ferrier, I.N. (Division of Psychiatry, Clinical Research Centre, Northwick Park Hospital, Watford Rd., Harrow HA1 3UJ, England) Tritiated LSD binding in frontal cortex in schizophrenia. Archives of General Psychiatry, 38(3): 278–280, 1981.

Tritiated LSD binding in the frontal cortex in schizophrenia was reinvestigated with saturation (Scatchard) analysis, which has the potential for revealing effects of residual drugs. There was no decrease in binding in the brains of 13 schizophrenic patients when compared with eight control brains. Quantities of neuroleptic remaining in the brain after death cannot be readily washed out and could have led to the previous report of reduced LSD binding. A decrease in affinity of LSD binding sites consistent with this possibility was demonstrated in chlorpromazine treated rats. In the brains of five patients who had probably been neuroleptic free for the year before death, tritiated LSD binding was significantly increased. It is concluded that this result must be replicated in larger samples. (17 references)—Author abstract, modified.

4606. Yaryura-Tobias, J.A. (Division of Research, North Nassau Mental Health Center, Manhasset, NY 11030) Anatomo-biochemical mapping of the brain: Neuropsychiatric correlations. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 466–469.

In a holistic approach to the etiophysiopathology of schizophrenia, the pharmacological, biological, and neurological considerations are discussed and the important role of brain mapping is emphasized. An overview of the following topics is presented: the biochemical theories of schizophrenia concerning the pharmacological actions of substances on neurotransmitters; psychomotor integration in mental illness; future applicability of brain mapping in the realm of psychiatry; the hypothesis that somatic changes in schizophrenia and those induced by psychotropic drugs are similar; the role of cerebral metabolic parameters and nutrition in brain pathology; and the separation between psychiatry and neurology. It is suggested that through brain mapping, a connection between the physical symptoms of schizophrenia and the relative concentrations and specific locations (at main anatomical sites) of neurotransmitters may be found. In combining the investigation of the neurology and etiophysiopathology of schizophrenia, it is hoped that a better understanding of the disease will be accomplished, and treatment of the patient will be of a holistic nature. (7 references)

4607. Young, M.A., and Meltzer, H.Y. (Department of Psychiatry, University of Chicago Pritzker School of Medicine, 950 East 59th Street, Chicago, IL 60637) RMI-81,582, a novel antipsychotic drug. Psychopharmacology, 67(1): 101–106, 1980.

RMI-81,582 (2-chloro-11-3-dimethylaminopropylidene morphanthridene), a potential antipsychotic agent, was administered to eight chronic and four acute male schizophrenics in an open label study. Ten of 12 patients improved regardless of whether they met research diagnostic criteria for acute or chronic schizophrenia. Significant improvement was noted on the Clinical Global Impressions and Brief Psychiatric Rating Scale. No extrapyramidal side effects were noted and other adverse reactions were few. Serum prolactin levels were increased by low moderate dosages of RMI-81,582 in 7 of 11 patients. Four patients had no increase in serum prolactin with RMI-81,582. In six of the seven patients who developed increases in serum prolactin, prolactin levels returned to those characteristic of the placebo period as the dosage of RMI-81,582 was increased. With classical neuroleptics, serum prolactin levels increase as the dose increases up to approximately the equivalent of chlorpromazine 600 mg/day and then remain fairly constant. The pattern of serum prolactin response in both man and laboratory animals and the absence of extrapyramidal side effects suggest RMI-81,582 may have a clozapine-like action. (27 references)—Author abstract.

Childhood Psychosis

4608. Juni, S. (No address given) The use of splitting in the analysis of childhood schizophrenia. American Journal of Psychoanalysis, 40(1):85–88, 1980.

The use of splitting in the analysis of childhood schizophrenia is described. Excerpts of a treatment summary involving a 6-month segment of psychoanalytically oriented therapy are presented. An 11-year-old schizophrenic boy was encouraged to use distancing to disorganize and not integrate the implications of analysis. The inherent tendency of a schizophrenic to separate himself from reality was used as a tool to check anxiety and allow analysis to proceed by minimizing cognitive and affective interferences. This enabled analysis to proceed with a minimum of disruptions until enough organization had been established within the sessions to attempt organization.

4609. Wolff, S., and Barlow, A. (Department of Psychological Medicine, Royal Hospital for Sick Children, 3 Rillbank Terrace, Edinburgh, Scotland) Schizoid personality in childhood: A comparative study of schizoid, autistic and normal children. Journal of Child Psychology and Psychiatry, 20(1):29–46, 1979.

Objective measures for the disturbance of affective relationships characterizing autistic and schizoid children were studied to validly differentiate schizoid children from well-functioning autistic and normal children. Schizoid children, high-grade speaking autistic children, and normal children, individually matched for age, sex, and intelligence, were compared on a variety of tests. In all cognitive, language, and memory tests, the schizoid children were more distractible than the normal group. In language function, the schizoid children showed similar disabilities to those of the autistic group, but to a lesser extent. Unlike autistic children, the schizoid children were not perseverative. On two tests of affect, the schizoid group used even fewer emotional constructs when describing people than did the autistics. These findings suggest that schizoid children can be differentiated by testing from autistic children and from normal children. (41 references) —Author abstract, modified.

Description

4610. Baxter, C.F., and Melnechuk, T. (Neurochemistry Laboratories, Veterans Administration Medical Center, Sepulveda, CA 91343) Perspectives in Schizophrenia Research. New York: Raven Press, 1980.

On the premise that schizophrenia comprises a family of different disease entities, approaches to the separation, identification, and characterization of these disease entities are discussed from the point of view of the neurophysiologist, neuroendocrinologist, psychopharmacologist, neurologist, neurochemist, morphologist, immunologist, behavioral psychologist, and clinician. Specific research problems such as experimental design, statistical analysis, drug side effects, placebo effects, patient selection, outcome measurements, and other parameters that may affect the onset and course of the disease are discussed. The genetic, emotional, and biological factors in the patient's internal environment, as well as occupational and social elements of the "external environment" that may be a predisposition for schizophrenic disease, are examined. Research directed toward the improvement of the health care delivery system for schizophrenic patients is also considered. The establishment of a regional brain bank for the collection of brains of deceased normal and schizophrenic individuals and the use of this material for research is described.

4611. Critchley, E.M.R.; Denmark, J.C.; Warren, F.; and Wilson, K.A. (Preston Royal Infirmary, Preston, Lancashire, England) Hallucinatory experiences of prelingually profoundly deaf schizophrenics. British Journal of Psychiatry, 138:30–32, 1981.

In a study of pseudoauditory experiences among deaf mental patients, 12 prelingually profoundly deaf schizophrenics were examined. Findings revealed that visual hallucinations occurred in 10 of the 12 people studied. Ten of the subjects also had experiences analogous to auditory hallucinations, although the voices may not have been heard. The results have implications for studies of communication in the deaf and show that deaf schizophrenics may present with symptoms analogous to those of the nuclear form of schizophrenia, even to the claim of hallucinations simulating those that are recognized as auditory in nature. (13 references)—Author abstract, modified.

4612. Huber, G. (Universitäts-Nervenklinik Bonn, Bonn, West Germany) Pure defect and its meaning for a somatosis hypothesis of schizophrenia. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 345–350.

Data obtained from 758 schizophrenic inpatients are reviewed in support of a new concept of pure defect, and its meaning for a somatosis hypothesis of the disorder is considered. The pure defect is characterized by lowering of the mental energy level, and the new typology reflects a revision of the doctrine that residual syndromes of schizophrenia are always psychopathologically different from chronic psychosyndromes of definable cerebral diseases. The data report the rate of occurrence of complaints and disorders in subjects experiencing pure residues, and demonstrates how these patients perceive their losses, suffer from them, and develop defense and compensatory mechanisms to cope with them. Findings from psychological tests show significant deviations from the norm in these patients, while echoencephalograms show a significantly higher average value of the transverse diameter of the third ventricle and a higher rate of pathological values than in patients with complete remissions. (18 references)—Author abstract, modified.

4613. Luftig, M.L. (California School of Professional Psychology, San Diego, CA 92199) Closing the revolving door: The experience of re-entering the community for the schizophrenic in remission. Dissertation Abstracts International, 40(8):3949–B, 1980.

The experiences of the schizophrenic in remission returning to the community after residence in a board and care home are described from interviews with five selected respondents who had resided in such a home for at least 2 months and who had been back in the community for at least 3 months. Transition from mental patient to community member seemed to occur in three stages: being for itself, being with others, and being in the world. Possible therapeutic applications are discussed including the implications of the research for individual and group psychotherapy; the use of the schizophrenic in remission as a paraprofessional counselor; and the usefulness of pastoral counseling with the schizophrenic in remission.—Journal abstract, modified.

4614. Muller, C. (Hôpital de Cery, Clinique-Psychiatrique Universitaire, Canton de Vaud, CH-1008 Prilly, Switzerland) The psychiatrist and schizophrenia—Reflections on an opinion poll among Swiss psychiatrists. Psychotherapie—Psychosomatik—Medizinische Psychologie. 30(1):10–14, 1980.

An opinion poll was conducted among Swiss psychiatrists concerning their views on the etiology of schizophrenia. Statistical evaluation of the questionnaires showed that 63.1 percent believe that it is impossible to set any priorities as to the importance of psychogenetic or hereditary neurobiochemical factors for the genesis of schizophrenia. Statistical analysis also showed that the age of the questioned psychiatrists correlated with the opinion which they formed regarding the genesis of schizophrenia. No statistically significant relationships were found between the occurrence of schizophrenic relatives in the family of the psychiatrists and their opinion on the etiology of schizophrenia. (16 references)—Journal abstract, modified.

4615. Niv, M.D. (900 West 190th St., New York, NY 10040) Schizophrenia: An existential approach. American Journal of Psychoanalysis, 40(1):43–52, 1980.

A phenomenological description is

presented of the experiences of 144 schizophrenic patients. The study revealed a crucial moral violation to be at the core of their symptomatology. A breach of the patient's inner moral code constituted the primary event to which the feelings of persecution and of being on trial are secondary. As defendants, these patients resorted to perjury, denied their acts, projected the blame, erected delusional justification systems, or changed their inner moral code. Some patients punished themselves; the majority withdrew into a prison of isolation. A nonjudgmental uncovering of their secret is the key to successful therapy with these patients. Sharing the experience with the therapist, the group, channeling their guilt into constructive actions, return to earlier beliefs, and a search for new ways to avoid old failings are the tasks confronting the therapist. (17 references)—Author abstract, modified.

4616. Owens, D.G., and Johnstone, E.C. (Northwick Park Hospital, Watford Road, Harrow, Middlesex HA1 3UJ, England) The disabilities of chronic schizophrenia—Their nature and the factors contributing to their development. British Journal of Psychiatry, 136(April):384–395, 1980.

Abnormalities currently present in 510 schizophrenic patients receiving long-term inpatient care were assessed and related to the earlier features of the illness, to personal and historical factors, and to physical treatments received. Subjects were examined in terms of their current mental state, cognitive functioning, neurological status, and behavioral performance. Significant associations between the present state and historical factors were few. Current abnormalities were not related to past physical treatment, but highly significant correlations were found between the impairments of the four areas of the present state. It is concluded that these impairments are likely to be an integral part of the disease. (32 references)—Author abstract, modified.

4617. Pansa, M. (Department of Psychology, Oxford University, Park Road, Oxford, England) Verbal conditioning of affect responses of process and reactive schizophrenics in a clinical interview situation. British Journal of Medical Psychology, 52(2):175–182, 1979.

Sixteen process schizophrenics and 16 reactive schizophrenic outpatients were compared on a verbal conditioning task in an alternating conditioning/extinction design, using verbal and nonverbal positive social reinforcement to influence the emission of self-referred affect statements. It was found that process subjects failed to condition during the time periods used, while reactives demonstrated a significant trials effect, showing trends consistent with those hypothesized from the type of design used. This differential conditionability between groups was shown not to be a function of diagnosis, sex, motivation, severity of illness, medication, hospitalization history, or general speech output. It was concluded that the degree of social responsiveness manifested in the premorbid history of the two groups is also operative in behavior during the psychotic period, specifically, in responsiveness to positive social reinforcers in a verbal conditioning task. (25 references)—Author abstract.

4618. Pilowsky, I., and Bassett, D. (Department of Psychiatry, University of Adelaide, Royal Adelaide Hospital, Adelaide, South Australia 5000, Australia) Schizophrenia and the response to facial emotion. Comprehensive Psychiatry, 21(3):236–244, 1980.

Responses to facial expression of emotion were investigated in 10 schizophrenic inpatients, 20 nonpsychotic psychiatric inpatients (neurotics and alcoholics), and 10 staff member controls. Analysis of data indicated that the schizophrenics produced the highest mean-word counts to all photographs (depicting fear, anger, joy, sadness, and neutral emotions), particularly for fear and anger. Failure to comment on affect, bizarre responses, comments on personal relevance of emotion depicted, and references to facial features occurred significantly more often in schizophrenic responses than in those of other groups. Also, schizophrenics were less likely than other groups to comment on the interior state of the depicted actor. Results are discussed in terms of a tendency to overarousal and abnormal processing apparent in schizophrenic responses. (25 references)

4619. Prosser, R.A. (University of Minnesota, Minneapolis, MN 55455) Reinforcement and hypohedonia in schizophrenia. Dissertation Abstracts International, 41(7):2777–B, 1981.

A deficit in reinforcement function in schizophrenia was hypothesized based on schizophrenics' many behavioral deficits, including deficits in learning, conditioning and performance tasks, decreased social involvement, flat affect, and hypohedonia. Schizophrenics and institutionalized nonschizophrenics were compared on indicated amount of pleasure derived from various activities, and amount of behavior maintained by different magnitudes of reinforcement in a simple operant task. The two groups did not differ in amount of indicated pleasure, but did differ on the latter variable in a manner supporting a reinforcement deficit in schizophrenia. For the total sample, subjects with a greater reinforcement deficit evidenced greater levels of psychopathology, poorer premorbid adjustment, and more physical hypohedonia. No conclusion could be reached as to whether schizophrenic reinforcement deficit is due to a high degree of psychopathology in general, or is specific to schizophrenia.—Journal abstract, modified.

4620. Reynolds, T.D. (Laboratory of Clinical Psychopharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032) Phase plane description of schizophrenic behavioral rhythms. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 285–293.

The utility of phase plane description of schizophrenic behavioral rhythms is discussed. Time series analysis of behavioral data collected from chronic schizophrenic patients reveals frequent occurrences of spectral density peaks in patients who do not show the qualitatively distinct phases of periodic catatonia. Patients have been observed for periods of 2, 5, 6, and 30 days. These cycles appear to be genuinely disabling because of the severity of the oscillation. Averaging techniques reveal wave forms of a characteristic shape, with steep rise and slower fall from a sharp peak, similar to one of the variables of the Volterra process. Since the generalized Volterra process, a two variable system where each derivative is a polynomial in the two variables, can be used to approximate a wide variety of nonlinear second order systems, it was selected as a starting point for modeling to simulate the observed cycles. (4 references) —Author abstract, modified.

4621. Rosen, A.J.; Tureff, S.E.; Daruna, J.H.; Johnson, P.B.; Lyons, J.S.; and Davis, J.M. (Department of Psychology, University of Illinois, Chicago, IL 60680) Pharmacotherapy of schizophrenia and affective disorders: Behavioral correlates of diagnostic and demographic variables. Journal of Abnormal Psychology, 89(3):378–389, 1980.

Time sampled observations were made of objectively defined ward behaviors in schizophrenic, affective, and schizoaffective patients during baseline and medication periods. Schizophrenics displayed less scanning, social interaction, participation, and laughing/smiling. The behavioral measures were relatively insensitive to demographic variables and were strongly dependent on environmental context. However, they did not change greatly over time for the major diagnostic categories in spite of pharmacological interventions that included therapeutic doses of antipsychotic, antidepressant, and antimanic drugs. Within diagnostic categories, patient clusters were extracted on the basis of amount and direction of behavior change. For affective patients, differential change was predictable from baseline response frequencies. The findings have implications for studies of dose response and rate dependence effects of psychotropic drugs in clinical populations, and may help resolve the responder/nonresponder controversy in pharmacopsychiatry. (51 references)—Author abstract, modified.

4622. Roy, A. (Clark Institute of Psychiatry, 250 College St., Toronto, Ontario M5T 1R8, Canada) Depression in the course of chronic undifferentiated schizophrenia. Archives of General Psychiatry, 38(3):296–297, 1981.

The hypothesis that parental loss before 17 years of age is a determinant of depression in the course of chronic schizophrenia was tested. Among 100 patients with chronic undifferentiated schizophrenia, parental loss before age 17 was significantly associated with the 39 who were treated for a depressive syndrome. It is suggested that patients with parental loss before age 17 may be more vulnerable to the development of depression. (11 references)—Author abstract, modified.

4623. Scheflen, A.E. (No address given) Levels of Schizophrenia. New York: Brunner/Mazel, 1981.

Schizophrenia is described on several levels of organization, beginning with the suprasystem of society and ending with the subsystem of molecular structure of the brain. A demonstration is given on how each level is cybernetically related to every other level and how processes at one level cause and maintain behavior at every other level. The societal perspective on psychosis and schizophrenia integrates historical views of madness with contemporary understandings of deviant behavior. The way the institutions of medicine, psychiatry, law, and education not only control, but maintain, deviance is shown. The next two social levels of organization—the family and the dyadic relationship, usually between mother and child—provide the environmental or communicational field in which schizophrenia can develop. The organizational level, including both bodily and physiological states and the actual behavior of the schizophrenic individual, is considered. The failure of classical psychodynamic and social psychological paradigms to explain schizophrenia is discussed, and recent advances in the neurosciences are used to describe schizophrenia at the levels of cerebral organization and neurosynaptic fields. (105 references)

4624. Sierra, M.R.; Lloret, E.; Lucas, R.; Perez, P.; Cano, J.; and Ribe, J. (Catedratico de Psiquiatria, Universidad de Valencia, Valencia, Spain) Objective observations in the study of schizophrenia. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 460–465.

Characteristics of schizophrenics using objective observations are discussed. When the schizophrenic is studied as an organism, peripheral observations show the organism's rejection of the world. These peripheral observations measure implicit and explicit behavioral types. The organism's centrality is measured by using bioelectrical rhythms in distinct cerebral areas. The observations are translated into objective data through the disciplines of biology and physics.

4625. Spohn, H.E., and Fitzpatrick, T. (Menninger Foundation, Box 829, Topeka, KS 66601) Informed consent and bias in samples of schizophrenic subjects at risk for drug withdrawal. Journal of Abnormal Psychology, 89(1):79–92, 1980.

The effect of informed consent screening on the findings of research in which schizophrenic patients are withdrawn from antipsychotic medication in order to eliminate the influence of drug treatment on dependent variables was studied. In order to determine the representativeness of a consenting sample of subjects, comparison was made to patients who did not participate in the research (no contact, refused by ward, and refused by self). Four hundred and twenty patients were screened for informed consent by both ward personnel and themselves, and 115 consented. Multivariate analyses of variance involving a multivariate vector on which 12 demographic, organismic, and course of illness variables were massed indicate that the final consenting sample differed significantly from the reference population from which it was drawn. Multiple regression analysis indicated that early relapsing, drug withdrawn patients differed significantly in prewithdrawal characteristics from later relapsing patients. (16 references)—Author abstract, modified.

4626. Watson, G.D.; Chandarana, P.C.; and Merskey, H. (Department of Psychiatry, University of Alberta, Edmonton, Alberta, T6G 2G3, Canada) Relationships between pain and schizophrenia. British Journal of Psychiatry, 138:33–36, 1981.

The phenomenology of pain was examined in 78 schizophrenic patients. A total of 29 subjects had current pain complaints. Of these patients, 13 had an appropriate physical cause, and 16 experienced pain of a seemingly psychological origin. The head, leg, and back were mentioned as the most common sites for pain. Complaints were most often described in sensory terms. Pain plausibly related to a specific delusion or hallucinatory process occurred only once, and no gross examples of insensitivity to noxious stimuli or to self-mutilation were seen. Patients with schizophrenia may have less pain than those with anxiety or depression, but the findings show that schizophrenics do experience pain both from physical and psychological causes. The influences of phenothiazines on pain experience is uncertain. (26 references) —Author abstract, modified.

4627. Weiman, M. (No address given) Schizophrenia: A Bibliography of Books in English. Darby, PA: Norwood Editions, 1981.

A bibliography of books on schizophrenia in English and an annotated listing of films dealing with schizophrenia are presented. The books are listed alphabetically according to their author, while the films are listed alphabetically according to their title. (870 references)

4628. Whitloc, F.A., and Bonfield, A.R. (Department of Psychiatry, University of Queensland, Royal Brisbane Hospital, Brisbane, Queensland 4029, Australia) Propranolol psychosis. Medical Journal of Australia, 1(4):184–185, 1980.

A case which illustrates typical features of a schizophrenic-like psychosis which may develop in patients being treated for hypertension with propranolol is presented. The patient had grandiose ideas and delusional beliefs and had been taking propranolol (80 mg twice daily) for hypertension. After 10 days of observation with no improvement, the propranolol medication was stopped and the psychotic symptoms disappeared within 6 days. Whether these hallucinatory states are caused by propranolol alone or by interaction with other drugs and alcohol cannot be decided at present, but it is suggested that if propranolol is to be used with phenothiazines to treat schizophrenic psychoses, it might be wise to caution the patient not to drink alcohol while taking these drugs. (7 references)

4629. Wolkinson, G.A. (No address given) Ego boundaries and paranoid delusions. Dissertation Abstracts International, 40(7): 3430–B, 1980.

The relationship between ego boundary impairment and the formation of paranoid delusions was investigated through an intensive case study of a male paranoid schizophrenic with different types of paranoid delusions. An attempt is made to generalize a classification of paranoid delusions according to their modes of operation as follows. 1) nondefensive paranoid delusions are those explained on the basis of impairment of ego boundaries; 2) core paranoid delusions are characterized by repetitive themes, by their imperviousness to structural therapeutic interpretations, and by the presence of actions aimed at promoting the paranoid delusional experience; 3) transmitted paranoid delusions are beliefs appropriated in an uncritical fashion from aggrandized parental objects; and 4) transferential paranoid delusions are delusional beliefs regarding important current objects which arise when representations of those objects are fused with archaic representations of early important objects, leading to a delusional perception of the current object. —Journal abstract, modified.

Diagnosis

4630. Arnold, O.H. (Psychiatric Clinic of Vienna, Vienna, Austria) Schizophrenic subtypes and some pathophysiological aspects. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 335–344.

Research on the pathophysiological aspects of schizophrenic subtypes is reported. Problems in the differential diagnosis of schizophrenia and other related psychoses are addressed, with emphasis on features of onset/attack, process, and exacerbation. It is suggested that in their longitudinal course the symptoms of the subtypes may be explained according to other biological criteria, as in the pathogenesis of tuberculosis, multiple sclerosis, or lupus erythematodes Examples of correlations of the new subtypes to parameters of energy-rich phosphates are provided. (14 references)—Author abstract, modified.

4631. Fowler, R.C.; Mezzich, J.; Liskow, B.I.; and Van Valkenburg, C. (Veterans Administration Medical Center (116A), 3350 La Jolla Village Dr., San Diego, CA 92161) Schizophrenia-primary affective disorder discrimination. II. Where unclassified psychosis stands. Archives of General Psychiatry, 37(7):815–817, 1980.

Cases of unclassified psychosis were assessed with a nine-variable diagnostic measure designed to discriminate schizophrenia and primary affective disorder. As a group, the unclassified cases occupied a midway position between and overlapping with cases of schizophrenia and primary affective disorder. Also, the mean discriminant function score of the unclassified group was significantly different from the mean scores of the groups with affective disorder and schizophrenia, although one subgroup of unclassified cases was statistically indistinguishable from the group with schizophrenia. While this investigation was essentially unsuccessful in reclassifying unclassified psychosis, a method for reclassifying diagnostic groups is demonstrated. The procedure is recommended for use in conjunction with followup and family studies as a basis for modifying diagnostic criteria. (14 references)—Author abstract.

4632. Fukuda, T. (Missouri Institute of Psychiatry, 5400 Arsenal St., St. Louis, MO 63139) Clinical-biologic delineation of schizophrenia, atypical psychoses, and paraphrenic psychoses. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 325–334.

Features of atypical psychoses, as compared with typical schizophrenia, are discussed. Various characteristics of paraphrenic psychoses are then examined to determine evidence for the existence of two groups of paraphrenias which differ with regard to hallucinations and delusions. The delineation of a clinical-biologic approach to these problems is also provided. It is concluded that at least three groups—typical, paraphrenic, and atypical schizophrenia—can be identified, and that these groupings should prove useful in future research on the etiopathogenesis of schizophrenic psychoses. (26 references)

4633. Gift, T.E.; Strauss, J.S.; Ritzler, B.A.; Kokes, R.F.; and Harder, D.W. (Department of Psychiatry, University of Rochester School of Medicine and Dentistry, 300 Crittenden Blvd., Rochester, NY 14642) How diagnostic concepts of schizophrenia differ. Journal of Nervous and Mental Disease, 168(1):3–8, 1980.

Nine different systems used for diagnosing schizophrenia were applied to a sample of 272 patients. The size and composition of the groups diagnosed as schizophrenic by each set of criteria were compared with respect to five clinical variables hypothesized to be important for differentiating the diagnostic systems. Results show that several of the variables tested distinguished schizophrenics diagnosed by some systems from those considered schizophrenic by other systems and from those patients in the sample not considered schizophrenic by any system. Those systems which tended to characterize patients classified as schizophrenic by either high levels of delusions of passivity, high psychosis scores, increased chronicity and low levels of affective symptoms, or by poor work and social function are identified. It is indicated that the various systems for diagnosing schizophrenia both have characteristic differences and areas of overlap. (16 references)—Author abstract, modified.

4634. Peake, T.H., and Albott, W. L. (Research and Education, Topeka State Hospital, Topeka, KS 66606) WIST predictions of brain damage: A follow-up to Albott and Gilbert. Journal of Clinical Psychology, 37(1): 180–182, 1981.

As a continuation of diagnostic issues raised by Albott and Gilbert (1973), the relative strengths and limitations of the Whittaker Index of Schizophrenic Thinking (WIST) as an indicator of brain damage were examined in 59 subjects. Specifically, the WIST demonstrated the power to avoid false predictions of brain damage and accuracy in predicting brain damage when the WIST signs were present. A substantial proportion of false negative predictions—no brain damage—indicates that WIST is not a test of or for organicity. (4 references)—Author abstract.

4635. Pueschel, K.M. (Memphis State University, Southern Ave., Memphis, TN 38152) Neuropsychological assessment and hypothesis testing in schizophrenic and brain-damaged patients. Dissertation Abstracts International, 40(7):3417–B, 1980.

Standard neuropsychological test measures and the hypothesis testing paradigm of M. Levine were used to investigate differences in cognitive functioning of schizophrenic, brain-damaged, and medical control patients. Use of the standard test measures resulted in numerous false positives among both schizophrenic and control groups, but did demonstrate differences in degree of impairment, primarily in comparisons of schizophrenic and brain-damaged patients. The hypothesis testing performance of the three groups showed that controls performed at more efficient levels than brain-damaged patients, while schizophrenics showed more variability and apparently used different methods of problem-solving. It is concluded that although the discrimination of schizophrenic from brain-damaged subjects by means of psychometric measures remains equivocal, qualitative differences in cognitive functioning do exist.—Journal abstract, modified.

4636. Silverstein, M.L., and Harrow, M. (Illinois State Psychiatric Institute, 1601 West Taylor St., Chicago, IL 60612) Schneiderian first-rank symptoms in schizophrenia. Archives of General Psychiatry, 38(3):288–293, 1981.

The relationships between Schneider's first rank symptoms (FRS) and major aspects of psychopathology were examined. Clinical course and outcome, indices of current functioning and symptom severity, premorbid adjustment, and prognostic indicators were assessed. Major comparisons were made between schizophrenic indicators with FRS at followup and schizophrenics with psychotic symptoms exclusive of FRS. Positive findings in select areas of outcome functioning favor the utility of FRS. However, several findings indicate that FRS were not more effective than non-Schneiderian psychotic symptoms in delineating central characteristics of the schizophrenic syndrome. They may identify a subgroup of schizophrenics with a more chronic course, but they do not appear to have the unique importance or diagnostic specificity that has been accorded them. (23 references)—Author abstract, modified.

4637. Strauss, J.S.; Bartko, J.J.; and Carpenter, W.T., Jr. (Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06519) New directions in diagnosis: The longitudinal processes of schizophrenia. American Journal of Psychiatry, 138(7): 954–958, 1981.

The longitudinal aspect of Kraepelin's concept of dementia praecox, or schizophrenia, is examined. It is emphasized that the field of psychiatry is presently attempting to deal with the complexities involved in psychopathology and its evolution—complexities that have been reemphasized by newer descriptive research methods. To account for patients' deviations from stereotyped diagnostic and prognostic concepts, multiple aspects of the course of the disorder have been defined and principles of multiaxial diagnosis have been supported. These principles can provide a basic structure for practice and research using a biopsychosocial orientation within the context of a systems model. (13 references)— Author abstract, modified.

Epidemiology

4638. Dohrenwend, B.S.; Dohrenwend, B.P.; Gottesman, I.I.; Link, B.; and Neugebauer, R. (School of Public Health, Columbia University, New York, NY 10027) Epidemiology and genetics of schizophrenia. Social Biology, 26(2): 142–153, 1979.

The need for epidemiological studies of broader populations to investigate the role of social and genetic factors in the etiology of schizophrenia is presented. Epidemiology and genetics must not only build on their separate achievements but also overcome problems in their research methods. One problem is that studies limited to treated cases may yield biased results. In the past variations in diagnostic criteria have led to confusing results in both genetic and epidemiologic research. It is suggested that future research use improved epidemiologic procedures now available and build on the strong epidemiologic finding of an inverse relation between social class and prevalence of schizophrenia to test genetic models by investigating class specific rates of disorder in particular kinds of relatives. (58 references)—Author abstract.

4639. Shimura, M., and Miura, T. (Department of Hygiene, Teikyo University School of Medicine, Itabashi-ku, Tokyo 173, Japan) Season of birth in mental disorders in Tokyo, Japan, by year of birth, year of admission and age of admission. Acta Psychiatrica Scandinavica, 61(1):21–28, 1980.

Seasonal distribution of births of schizophrenic and manic-depressive patients born in Tokyo between the years of 1841 and 1940, and first admitted between 1879 and 1973, was examined by year of birth, year of first admission, and age at first admission. In both mental disorders, an autumn excess of births was observed among those born up to the latter part of the 19th century, after which the distribution changed to show a spring excess. Findings suggest that the distributional pattern depended upon both year of birth and year of admission, rather than age at first admission. (24 references)—Author abstract, modified.

The Family

4640. Marquart, M.E. (California School of Professional Psychology, Los Angeles, CA 90053) Separation-individuation and communication variables in families with a schizophrenic adolescent compared to families with a nonschizophrenic adolescent. Dissertation Abstracts International, 40(8):3950–B, 1980.

The relevance of communication processes and separation anxiety to the formation of identity was investigated. The results suggest that families with schizophrenic adolescents can be characterized by significantly higher degrees of separation anxiety. These families are symbiotically attached and unable to function as separate individuals. The communication in these families serves to perpetuate this symbiosis, fostering an environment wherein no one member is recognized as autonomous or independent. It is tentatively suggested that communication processes and separateness communicate in ways that render autonomy impossible, which in turn only enhances the families' symbiotic attachments.—Journal abstract, modified.

4641. Wynne, L.C. (Department of Psychiatry, University of Rochester, 300 Crittenden Blvd., Rochester, NY 14642) Poor family communication and schizophrenia. In: Corfman, E., ed. Families Today—A Research Sampler on Families and Children. Washington, DC: Superintendent of Documents, U.S. Government Printing Office, 1979. pp. 709–724.

The influence of unusual styles of family communication on the development of schizophrenia was investigated. One hundred and fifty families were under observation from the time a son, who was 4, 7, or 10 years of age, entered treatment. In all families, one parent had been diagnosed as schizophrenic or as having another psychiatric illness. Peculiarities in communication were classified into 32 categories, and underlying many of them was the speaker's inability to maintain attention to the subject at hand or to the demonstration of attentional repetition. A relationship occurred between level of vagueness and ambiguity in parental communication and the schizophrenic offspring's subsequent breakdowns. This finding suggests that deviant communication can contribute to chronic schizophrenia. It is concluded that such a problem adds to a child's genetic vulnerability rather than triggers the disorder. In addition, the children of parents with deviant communication styles had more problems in school than other children.—Journal abstract, modified.

Genetics

4642. Angst, J.; Felder, W.; and Lohmeyer, B. (Research Department, Psychiatric University Clinic, Zurich, Switzerland) A genetic study on schizoaffective disorders. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 12–18.

A group of 150 schizoaffective probands and 1,004 first-degree relatives were examined in a study of heterogeneity in this disorder. The probands were separated into manic and nonmanic groups. Relative morbidity did not differ significantly between groups, and a second attempt to break down the probands into affect-dominant and schizo-dominant cases was also unsuccessful. The morbidity risk in both groups was generally the same. There was a mild trend favoring a slightly higher risk for schizophrenia in schizo-dominant probands and a higher risk for affective disorder in affect-dominant probands. It is concluded that schizoaffective disorders cannot be subsumed either to schizophrenia or affective disorders, and that, from the genetic viewpoint, the international classification of these schizoaffective disorders is not supported. (9 references)—Author abstract, modified.

4643. Angst, J., and Scharfetter, C. (Psychiatric University Clinic Zurich, Research Department, Zurich, Switzerland) Subtypes of schizophrenia and affective disorders from a genetic viewpoint. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 351–357.

Heterogeneity in schizophrenia and affective disorders was studied using the morbidity risk of first-degree relatives as a criterion for homotypology. It was found that within schizophrenia, the secondary cases in relatives are mostly schizophrenic, while those in unipolar and bipolar depression are generally affective. The schizoaffective group does not fit into either category. From a genetic standpoint, hebephrenic and paranoid schizophrenics are the best defined nosological subgroups, and the catatonic subtype is of special interest, because it may take a nosological position between schizophrenia and affective disorders. An especially close relationship between schizoaffective disorders and catatonic schizophrenia is also noted. (11 references)—Author abstract, modified.

4644. Debray, Q.; Caillard, V.; and Stewart, J. (Hôpital Necker and C.E.T.S.A.S., Paris, France)

Testing genetic models of schizophrenia: The simulation of pedigree data. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 19–22.

The use of simulated pedigree data to test genetic models of schizophrenia is reported. Results are reported from application of the method to 25 pedigrees of schizophrenic patients comprising a total of 1,333 individuals. Six genetic models were studied. The findings show that the likelihood surface obtained with real data is flat and fails to distinguish between the one, two, and four locus models. This suggests that the etiology of schizophrenia is heterogeneous or even nongenetic. However, a simple model with a single completely recessive locus and incomplete penetrance in the homozygote also produced a flat likelihood surface. This single locus model is presented as a potentially useful working hypothesis. (6 references)—Author abstract, modified.

4645. Mendlewicz, J.; Linkowski, P.; and Wilmotte, J. (Erasme Hospital, Department of Psychiatry, Free University of Brussels, Brussels, Belgium) Relationship between schizoaffective illness and affective disorders or schizophrenia: Morbidity risk and genetic transmission. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 406–411.

Family studies were conducted to investigate genetic factors in the etiology of schizoaffective illness, which has been linked to schizophrenia and to affective disorders and has been suggested as a separate disease type. Morbidity risks for affective illnesses and schizophrenia were estimated in the first-degree relatives of schizoaffective probands as compared to matched controls—bipolars, unipolars, and schizophrenics. The results indicate that schizoaffective illness is a heterogeneous entity. This syndrome appears primarily related to the affective disorders, but there may be a subgroup linked to the schizophrenic spectrum disorders. (20 references)—Author abstract, modified.

4646. Quitkin, F.M.; Rifkin, A.; Tsuang, M.T.; Kane, J.M.; and Klein, D.F. (New York State Psychiatric Institute, 722 West 168 St., New York, NY 10032) Can schizophrenia with premorbid asociality be genetically distinguished from the other forms of schizophrenia? Psychiatry Research, 2(1):99–105, 1980.

To determine whether chronic schizophrenia with premorbid asociality (SPA) has a genetic basis, the risk of schizophrenia was examined among relatives of probands who did not meet the criteria for SPA. Results show that the incidence of schizophrenia in relatives of SPA probands was lower than that in relatives of non-SPA probands. This difference approached statistical significance. However, because most studies have found a higher familial genetic loading in chronic forms of schizophrenia, the nonsignificant trend noted for SPA patients to have fewer ill relatives is contrary to expectations and suggests that they are a subgroup with a nongenetic etiology. (24 references)—Author abstract, modified.

High-Risk Studies

4647. Simons, R.F. (Department of Psychology, University of Delaware, Newark, DE 19711) Electrodermal and cardiac orienting in psychometrically defined high-risk subjects. Psychiatry Research, 4(3):347–356, 1981.

Electrodermal and cardiac orienting behavior was investigated in three groups of subjects defined as schizotypic on the basis of their responses to Chapman's psychometric instruments for the assessment of personality characteristics thought to be closely associated with schizophrenia. Psychometrically defined subjects—anhedonic, perceptual aberration, and control—were examined for orienting and habituation to simple auditory stimuli. Results support the hypothesized continuity between anhedonic subjects and the autonomically hyporesponsive group of patients frequently described in the literature on schizophrenia. Results are discussed with reference to identification of populations at risk for schizophrenia and in light of recent appeals to identify biologically homogeneous subgroups of schizophrenic patients. (34 references)—Author abstract, modified.

Prognosis

4648. Brockington, I.F.; Kendell, R.E.; and Wainright, S. (Illinois State Psychiatric Institute, 1601 West Taylor St., Chicago, IL 60612) Depressed patients with

schizophrenic or paranoid symptoms. Psychological Medicine, 10(4):665–675, 1980.

Family history, response to treatment, and outcome were investigated in 76 patients with both depression and schizophrenic or paranoid symptoms. The patients were highly heterogeneous in history, clinical picture, and outcome. Many followed a typical schizophrenic course, and others a typical course for affective disorders; but only four were given a final diagnosis of manic-depressive disease. The best predictors of poor outcome were a mode of onset as an exacerbation of previous psychotic symptoms and the presence of schizophrenic symptoms at some time without depression. The best predictors of good outcome were Stephens' criteria of good prognosis schizophrenia and Kasanin's concept of acute schizoaffective psychosis. The findings suggest a continuum of outcome between schizophrenia and unipolar depressive psychosis. (20 references)—Author abstract, modified.

4649. Brown, W.A., and Laughren, T. (VA Medical Center, Davis Park, Providence, RI 02908) Low serum prolactin and early relapse following neuroleptic withdrawal. American Journal of Psychiatry, 138(8):237–239, 1981.

Research evidence is reported from a study of 28 schizophrenic patients over 10 months to demonstrate that those with low serum prolactin concentrations during maintenance neuroleptic treatment relapse earlier than those with higher serum prolactin concentrations. Although the relative bioavailability of neuroleptics would appear a likely explanation, the data do not support this hypothesis. The findings suggest that some patients have a modest prolactin rise at the onset of treatment, show a marked diminution with continued treatment, and tend to early relapse when neuroleptic is discontinued. Others have a more robust increase at onset, show a less dramatic drop during treatment, and remain clinically stable for a longer period of time after withdrawal. These two groups may have a different neurophysiologic substrate that underlies differences in prolactin regulation and clinical course. (10 references)

4650. Glosz, J.T., Jr., and Grant, I. (Department of Psychiatry (M-003), University of California, San Diego, La Jolla, CA 92093) Prognostic validity of the MMPI. Journal of Clinical Psychology, 37(1):147–151, 1981.

An attempt was made to determine the prognostic validity of the Minnesota Multiphasic Personality Inventory (MMPI) for 41 psychiatric patients diagnosed as schizophrenic. Patient records were analyzed with multiple regression techniques using the MMPI scales as the independent variable and length of hospital stay as the dependent measure. It was found that certain MMPI scales are highly significant and powerful predictors of length of hospital stay, which indicates that the MMPI does indeed have validity as a quantitative predictor of prognosis in clinical situations. Particularly, the two scales with the highest predictive power, schizophrenia and depression, were inversely related concerning clinical outcome. (17 references)—Author abstract.

4651. Gross, G., and Huber, G. (Abteilung für Psychiatrie und Neurologie der Medizinischen Hochschule Lubeck, Lubeck, West Germany) Genetic conditions and prognosis in schizophrenia. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 23–28.

A group of 758 schizophrenic patients were studied with emphasis on the development of the disorder and its social psychiatric aspects. Data obtained from a 22.4 year followup of 502 probands indicate that 22.1 percent of the subjects experienced psychopathologically complete remissions. Noncharacteristic and characteristic residual syndromes occurred in 43.2 percent of the subjects. An affliction with schizophrenia in blood relationship was found in 30 percent of the cases. In 5.2 percent of the subjects, cyclothymia was present and 20.7 percent evidenced diagnostically unclear endogenous psychoses. Presence or absence of familial affliction had no influence on long-term prognosis with one exception. Even a high affliction with two or more secondary cases of schizophrenia in blood relationships did not adversely affect the prognosis.—Author abstract, modified.

4652. Gross, G., and Huber, G. (Abteilung für Psychiatrie und Neurologie der Medizinischen Hochschule Lubeck, Lubeck, West Germany) Types of course of schizophrenia. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 396–401.

Followup data on 502 German schizophrenics who were hospitalized from 1945 to 1959 were reviewed to identify empirically demonstrable types by combining course of the disease with the different types of psychopathological remissions. Of the 72 categories that were determined, 12 basic types were identified by combining similar types, classified according to the rate of social cure. In the most favorable group, 100 percent were socially cured and fully employed. In the relatively favorable group, the rate of social cure was still markedly above the rate of cure for the entire group, while the rate in the unfavorable group was below the total rate. The most unfavorable type leads to typically schizophrenic psychoses and was found in 4 percent of the cases. These psychoses developed within 3 years after disease onset and persisted until late catamnesis. (1 reference)—Author abstract, modified.

4653. Huber, G. (Universitäts-Nervenklinik Bonn, Bonn, West Germany) Long-term investigation on course and prognosis of schizophrenic illnesses. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 389–395.

Followup studies on 502 German schizophrenics who were hospitalized from 1945 to 1959 are reviewed to report disease course and prognosis. After an average of 22.4 years, the subjects showed complete psychopathological remission in 22.1 percent of the cases, while 56.2 percent of the subjects were socially recovered, 86.7 percent were living at home, and 13.3 percent were permanently hospitalized. The prognostic meaning of anamnestic, clinical, and therapeutic data was examined, and the results led to revision of concepts of schizophrenia which do not consider the patients' external worlds. The revision proposes a disease which is genetically and somatically founded, which displays a cerebral enzyme defect functioning via neurobiochemical mechanisms, and which is partly determined by environmental conditions and susceptible to nonspecific stress. (1 reference)—Author abstract, modified.

4654. Saito, M. (Department of Psychiatry, Kansai Medical University, Osaka, Japan) CEEG study on patients under the psychiatric drug treatment: The correlation between EEG alteration and clinical evolution. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. B. Amsterdam: Elsevier/North Holland, 1979. pp. 1306–1311.

A group of 60 schizophrenic and 40 depressed patients were followed up electroencephalographically and clinically to determine possible differences between responsive and resistant cases to psychotropic drug treatment. The drugs included haloperidol, perphenazine, or chlorpromazine for schizophrenia and amitriptyline or imipramine for depression. Therapy responsive patients presented markedly different changes in EEG from resistant patients either in 3 hours or 1-week postdrug regardless of the given drug. A gradual increase of slow waves suggests the patient's resistance to treatment. It is concluded that an early prediction of clinical outcome can be objectively achieved through the study of EEG alteration. (2 references)—Author abstract, modified.

4655. Zigler, E., and Levine, J. (Department of Psychology, Yale University, Box 11A Yale Station, New Haven, CT 06520) Premorbid competence in schizophrenia: What is being measured? Journal of Consulting and Clinical Psychology, 49(1):96–105, 1981.

The Zigler-Phillips premorbid social competence scale was evaluated on whether it assesses one or several dimensions in patient groups differing in regard to gender and type of hospital. The groups investigated were VA hospital male, state hospital male, and state hospital female schizophrenic patients. For all groups, the competence scores reflected three orthogonal factors, but the factorial structure differed as a function of gender and type of hospital. One factor in all groups was defined by the usual socioeconomic variables of education and occupation. Each of the five scale indices was found to make an independent contribution to the variance of the overall competence score, but the education index had a smaller role than the other four measures. Female patients had higher competence scores than state hospital males—a difference that was not due to the marital status variable alone. Possible explanations for this finding are discussed and suggestions are made for refinement and further development of the scale. (62 references)—Author abstract.

Psychological Theory

4656. Brown, S. (Department of Psychiatry, Western Psychiatric Institute, University of Pittsburgh School of Medicine, 3811 O'Hara St., Pittsburgh, PA 15261) Dissociation of pleasure in psychopathology. Journal of Nervous and Mental Disease, 169(1):3–17, 1981.

The development of the concept of dissociation from 19th century psychological theory through 20th century neurophysiological thought is analyzed. Recent research, indicating that normal individuals show an association between emitted pleasurable behavior and self-perception of pleasurable activity, whereas depressives and schizophrenics show a lack of association, or dissociation, between these measures, is discussed. Concomitantly, depressives show an abnormal degree of association between the experience and expression of negative affect. Such a discrepancy in systems of affect is considered as both an important pathological element in mental disorder and also as a valuable new research tool for studying etiology, differential diagnosis, and therapeutic efficacy in psychobiological illness. (137 references)—Author abstract.

4657. Faguet, R.A. (1800 Fairburn Ave., Los Angeles, CA 90025) Space, symmetry, and psychosis. American Journal of Psychoanalysis, 40(1):89–90, 1980.

The concept that the spherical and symmetrical model of the universe can be related to the major psychoses is presented. Since normal mental activity reflects a symmetrical internal organization, the major psychoses can be characterized as primary disturbances in space/time configuration. Schizophrenia is described as a disorder of the left hemisphere and a disorder of finitude. Manic depression is a disorder of the right hemisphere and hence a disorder of spatial thought. Studies are briefly cited to support the hypothesis that schizophrenia and affective illness evolve from distinct hemispheric disorders.

4658. Glass, J.M. (Department of Government and Politics, University of Maryland, College Park, MD 20742) Facts and meaning: From the perspective of schizophrenic internality. Contemporary Psychoanalysis, 17(1):118–135, 1981.

Paul Ricoeur's (1977) conception of the status of psychoanalysis as a science is examined within the context of intersubjective recognition, what intersubjectivity implies for understanding the symbol productions of schizophrenic language, and what the scientific claims of psychoanalysis reveal about the origin of psychic facts and their representation in language. Ricoeur's arguments, and their similarities to propositions put forth by Harry Stack Sullivan, are reviewed and discussed in the areas of consensual validation of meaning, truth claims in psychoanalysis, the nature of communication and the significance of symbolic language, psychic facts of psychoanalysis and their investigation, the structures of the linguistic self, and the productions of the inner world and the interpretation of reality. Finally, general issues which a psychoanalytic view of the mind poses for social scientists and political scientists, in particular, are raised. (10 references)

Treatment

4659. Berger, P.A., and Davis, K.L. (Stanford Psychiatric Clinical Research Center, VA Medical Center, Palo Alto, CA 94304) Pharmacological studies of tardive dyskinesia: Implications for future research. In: Baxter, C., ed. Perspectives in Schizophrenia Research. New York: Raven Press, 1980. pp. 333–351.

Pharmacological studies of the side effects of tardive dyskinesia are reviewed. The reasons for a carefully designed, multicenter prospective study to address the question of tardive dyskinesia are presented. Areas covered include: epidemiology of tardive dyskinesia, differential diagnosis, neuropharmacology of tardive dyskinesia, pharmacological studies in humans with tardive dyskinesia, and unanswered questions concerning tardive dyskinesia. The discussion that followed the presentation of the paper at a symposium for strategies for future research in schizophrenia is given. (87 references)

4660. Brajsa, P.; Ozimec, J.; and Baldauf, J. (Radna jedinica za zivcane i dusevne bolesti Psihijatr. odjela Medicinskog centra, Varazdin, Yugoslavia) Review of community outpatient service for schizophrenics in Varazdin. Socijalna Psihijatrija, 7(4): 397–406, 1979.

A therapeutic community of about 150 schizophrenic patients receiving outpatient treatment in

Varazdin, Yugoslavia is described, with emphasis on the experiences of the last 10 years. The patients are in social remission and have access to the outpatient unit once a week, where they have the opportunity for relaxed contacts and therapeutic relationships with the psychiatrists, psychologists, or nurses. Large and small groups of patients, family groups, dyads, and individual counseling are used. Outside social activities are included, and a special bulletin is published. The basic goal of the program is to achieve qualitative and long-lasting remission and short hospitalization during relapses. Emphasis is on change in relationships, communication, and defense mechanisms, rather than changes in the individual himself and his symptoms. Therapeutic techniques are based on the principles of natural family systems and groups. (12 references)—Journal abstract, modified.

4661. Cancro, R.; Davis, J.M.; Klawans, H.; and Tancredi, L. (New York University Medical Center, 566 First Avenue, New York, NY 10016) Medical and legal implications of side effects from neuroleptic drugs. A round-table discussion. Journal of Clinical Psychology, 42(2):78–82, 1981.

In a round-table discussion, the side effects that may occur during the treatment of schizophrenia with neuroleptic drugs are fully examined. Included are autonomic, extrapyramidal, other CNS, endocrine, and metabolic, allergic, and skin and eye side effects. The differences between the various side-effect profiles of various antipsychotic drugs are noted. The restrictions imposed by laws designed to protect the patient's rights are evaluated with regard to the side effects of neuroleptic drugs. The meaning of informed consent is delineated.—Author abstract, modified.

4662. Cmelic, S., and Henig, L. (Psihijatrijska bolnica, Ugljan, Yugoslavia) EEG and psychological (Rorschach) monitoring of electroconvulsive therapy in schizophrenic patients. Psihijatrija Danas, 11(3-4): 427–433, 1979.

A group of 17 schizophrenic patients who received electroconvulsive therapy (ECT) was monitored by means of EEG, Rorschach's psychodiagnostic test, and the Itil-Keskiner rating scale. During and immediately after the therapy, reactions of patients indicated transitory deterioration which was mostly expressed on EEG, less on the Rorschach, and least in clinical observations. Twenty-one days after therapy had been terminated, all findings were notably improved. However, the EEG and, in part, the Rorschach findings were not fully normalized, although they showed a tendency toward improvement. Further monitoring of schizophrenic patients is necessary using the same research technique in order to gain insight into the process of normalization in the organic and psycho-organic domain and, additionally, to detect possible aggravations in the domain of psychic epiphenomena which are always possible in chronic schizophrenic patients. (2 references)—Journal abstract.

4663. Corkin, S.; Twitchell, T.E.; and Sullivan, E.V. (Department of Psychology, Massachusetts Institute of Technology, Cambridge, MA 02139) Safety and efficacy of cingulotomy for pain and psychiatric disorder. In: Hitchcock, E., ed. Modern Concepts in Psychiatric Surgery. Amsterdam: Elsevier/North Holland, 1979. pp. 253–272.

A prospective study of therapeutic outcome, neurologic status, and behavioral test performance, carried out with 57 patients who received bilateral stereotactic anterior cingulotomy for the relief of intractable pain or psychiatric disorder, is described. The therapeutic outcome of 34 patients was evaluated at two times about a year apart; the incidence of improvement was 64 percent at the first assessment and 71 percent at the second, suggesting that their postoperative conditions were relatively stable. When the total group of 57 patients was subdivided according to diagnosis, the incidence of improvement was high in patients with persistent pain and also in those with depression, but low in those with a diagnosis of schizophrenia or obsessive-compulsive neurosis. Significant gains in Wechsler IQ and, for patients under 30 years of age, in a nonverbal fluency task are reported. In the early postoperative period, patients over 30 years showed significant losses on an embedded figures task and in copying a complex drawing, while men, but not women, showed a decline on two tapping tasks. It is noted that there is no evidence of lasting neurologic or behavioral deficits after cingulotomy. (37 references)—Author abstract, modified.

4664. Davis, N.J., and Mathews, A.T. (Harvard University, Boston,

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MA 02138) An integrated approach to social skills training for schizophrenic clients in a day treatment setting. Dissertation Abstracts International, 41(8): 3157–B, 1981.

The relative effectiveness of an integrated social skills program—a traditional program based on structured learning theory—and a discussion group—a variant of psychodynamic group therapy—was examined with schizophrenic clients in a day-treatment setting. Pretest, posttest, and 1-month followup assessments were made measuring adjustment, social behavior, cognitive processes, egocentricity of thought, state anxiety, self-acceptance, sense of well-being, sociability, and social presence. Significant change for all groups combined was demonstrated in a number of variables. There were virtually no differences when the treatment groups were compared to each other or when independent variables such as age, sex, education, and length of time in treatment were considered. Findings indicate positive change over time in humor, social skills, level of cognitive functioning, self-acceptance, and sociability.—Journal abstract, modified.

4665. Elizur, A.; Segal, Z.; Yeret, A.; Davidson, S.; and Atsmon, A. (Shalvata Psychiatric Center, POB 94, Hod Hasharon, Israel) Antipsychotic effect of propranolol on chronic schizophrenics: Study of a gradual treatment regimen. Psychopharmacology, 60(2):189–194, 1979.

Ten chronic treatment-resistant schizophrenic patients were treated in a single-blind trial for 6 weeks with propranolol in daily doses of up to 3 g, to evaluate a modified dose regimen of propranolol treatment in these patients. Four of the patients improved significantly and could be released from the hospital, regaining premorbid social and work adjustments. The modified regimen proved safe as long as the dose increment was not more than 80 mg per day. The mean therapeutic level of propranolol was 1,600 mg per day, which proved to be a safe dose. Although three patients with hypertensive encephalopathy responded, their response was not related to the maximum dose but to a drastic change in the rate of the dose increase. It seems that on the basis of these results a double-blind comparative study would be worthwhile. (10 references)— Author abstract, modified.

4666. Fraser, I.G.P. (No address given) Dealing with the disadvantaged: Understanding schizophrenics. British Medical Journal, 6273:1377, 1981.

Concerns and problems of the schizophrenic patient are discussed in order to assist doctors and other staff members in dealing with them. It is suggested that doctors should encourage trust in themselves by employing the proper tone of voice, direct statements, and straightforward replies. At all times the schizophrenic patient should be regarded as an individual and his suffering should be recognized.

4667. Freeman, H.L. (Hope Hospital, Eccles Old Road, Salford M6 8HD, England) Long-term treatment of schizophrenia. Comprehensive Psychiatry, 22(1): 94–102, 1981.

Issues in the long-term treatment of schizophrenia are examined from a biopsychosocial perspective. Results of an English study of 190 chronic schizophrenics suggest that interaction between drug side effects, environmental stimuli, and psychophysiological sensitivity may contribute to relapse in deinstitutionalized patients, despite maintenance of apparently adequate levels of medication. The role of neuroleptics in long-term treatment is considered in terms of their influence on patterns of service delivery, their efficacy in preventing acute relapses, and their impact on the overall prognosis of schizophrenia. Evidence is now available which indicates that the prognosis of schizophrenia can be considerably improved by neuroleptic maintenance therapy, particularly with the new depot drugs. It is concluded that medical efforts must be related to social and occupational rehabilitation and applied with skill and care in an integrated and comprehensive fashion. (20 references)

4668. Imlah, N.W. (All Saints' Hospital, Birmingham, England) Long-term effects of pipothiazine palmitate. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. B. Amsterdam: Elsevier/North Holland, 1979. pp. 1081–1086.

The long-term effects of pipothiazine palmitate on 15 schizophrenic patients were investigated. The therapeutic results were particularly impressive since many of the subjects had a poor prognosis prior to treatment. There was an absence of schizophrenic symptoms in half of them at several followup ratings, including a 5-year evaluation. No serious side effects were noted, and patients were satisfactorily maintained at a lower level than that suggested in most short-term studies. In common with the 5-year followup of fluphenazine decanoate, there appear to be no unforeseen or undue hazards in patients on long-term maintenance with depot neuroleptics in moderate dosages (up to 100 mg per injection). (2 references)

4669. Judd, L.L.; Janowsky, D.S.; Segal, D.S.; Parker, D.C.; and Huey, L.Y. (Department of Psychiatry (M-003), University of California at San Diego, La Jolla, CA 92093) Behavioral effects of methadone in schizophrenic patients. American Journal of Psychiatry, 138(2):243–245, 1981.

Initial data are reported from a placebo-controlled, double-blind investigation of the effects of methadone on the behavior of six schizophrenic patients. No significant baseline differences were found between methadone and placebo days. Methadone produced a small but definite motor slowing and promoted lethargy, deactivation, and loss of function. Negative schizophrenic symptomatology—emotional withdrawal, motor retardation, and blunted affect—increased after methadone administration. An increase in prolactin was noted, probably due to the mediation by the brain of opiate receptors that inhibit dopamine release from the tuberoinfundibular dopaminergic neurons. The data also suggest that methadone hydrochloride does not exert a specific antipsychotic effect in schizophrenic patients but instead accentuates emotional withdrawal and decreases motor activity. (12 references)

4670. Kessler, K., and Waletzky, J.P. (2020 K St., NW, Suite 810, Washington, DC 20006) Clinical use of the antipsychotics. American Journal of Psychiatry, 138(2): 202–209, 1981.

Current practical information on the clinical management of acute episodes and maintenance therapy in schizophrenia, including dosage schedules, plasma level determinations, and side effects—tardive dyskinesia and reversible extrapyramidal syndromes—is reviewed. All neuroleptics given in equivalent doses produce about the same degree of antipsychotic activity. The most common cause of treatment failure in patients with acute psychosis is an inadequate dose, and the most common cause of relapse is patient noncompliance. It is concluded that maintenance medication should be given at the lowest dose that will sustain improvement. Several new alternative drug treatments are also discussed. (68 references)—Author abstract, modified.

4671. Lapierre, Y.D.; Berliss, H.; Monpremier, P.; and Elie, R. (Department of Psychiatry and Pharmacology, University of Ottawa, 197 Cumberland St., Ottawa, Ontario, Canada) Methodology and results of a long-term study of long-acting neuroleptics: Pipothiazine palmitate and fluphenazine decanoate. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. B. Amsterdam: Elsevier/North Holland, 1979. pp. 1087–1094.

A one-year study comparing fluphenazine decanoate and pipothiazine palmitate administered parenterally at 4-week intervals in the prophylactic treatment of 43 chronic ambulatory schizophrenics is presented. Dosage requirements of pipothiazine palmitate were slightly greater than those of fluphenazine decanoate in a ratio of 4:3. The overall efficacy index was slightly higher for pipothiazine palmitate than for fluphenazine decanoate. Sex and drug interactions were common throughout the study, suggesting some instances of superior efficacy for one drug or the other at different items of the Brief Psychiatric Rating Scale. These sex and drug interactions suggest that pipothiazine palmitate may produce better results in males and that fluphenazine decanoate may be more beneficial in females. (5 references)—Author abstract modified.

4672. Manos, N.; Gkiouzepas, J.; and Logothetis, J. (Karolou Diehl 20, Thessaloniki, Greece) The need for continuous use of antiparkinsonian medication with chronic schizophrenic patients receiving long-term neuroleptic therapy. American Journal of Psychiatry, 138(2):184–188, 1981.

A group of 98 chronic schizophrenic patients receiving long-term neuroleptic treatment and trihexyphenidyl were reassigned to either placebo or trihexyphenidyl in a double-blind 6-week study. Fifty-one (68 percent) of the 75 subjects given placebo developed severe worsening of extrapyramidal signs, which resulted in their discontinuation in the study. Twenty-one (28 percent) of the placebo, but only two

(8.7 percent) of the trihexyphenidyl subjects developed less severe symptoms. Furthermore, 50 (66.6 percent) of the placebo patients, but only two (8.7 percent) of the trihexyphenidyl subjects had psychotic or other severe physical symptoms related to withdrawal of prestudy antiparkinsonian medication. These data support the need for continuous use of antiparkinsonian medication in the long-term neuroleptic therapy of chronic schizophrenic patients. (20 references)—Author abstract, modified.

4673. Muacevic, V., and Marangunic, M. (Medicinskogfakultetatsihiatrijska klinika, Zagreb, Yugoslavia) Group psychotherapy of schizophrenics. Socijalna Psihijatrija, 7(4):361–367, 1979.

The historical development of group psychotherapy with schizophrenic patients is examined with special attention to selection of patients and indications and counterindications. Transfer and countertransfer are shown as the most frequently encountered difficulties in group work as well as confusion and disorientation during group work, fears and discouragement among therapists, and the therapist's personality. Various forms of resistance and group interactions are explained, and various techniques are described, along with the relations of psychotherapy to psychopharmacotherapy and the influence of the environment and contemporary concepts in psychiatry upon group psychotherapy with psychotics. (27 references)—Journal abstract, modified.

4674. Muller, E. (Universitäts-Nervenklinik mit Poliklinik, Erlangen, West Germany) Diagnosis and treatment of acute schizophrenic psychoses. Neurologie und Psychiatrie für die Praxis, 5:89–91, 1979.

Examples of the onset and symptoms of acute schizophrenic psychoses of various types are presented, and their diagnosis and treatment are discussed. Emphasis is placed on the danger of the patient's harm to himself or others during paranoid hallucinatory states. The necessity of immediate hospitalization is emphasized, even if it is against the will of the patient or his family. A wide spectrum of manic experiences leading to stupor is illustrated. Therapy with neuroleptics is discussed.—Journal abstract, modified.

4675. Neumann, N.U. (Abteilung für Psychiatrie II, Krankenhaus Gunzburg, Ulm, West Germany) The treatment of schizophrenic psychoses with hemodialysis. Fortschritte der Medizin, 97:654–658, 1979.

The treatment of schizophrenic psychoses with hemodialysis is investigated. Three presently disputed hypotheses are examined. There is no uniform method of deducing therapeutic experiences or therapeutic indications that are involved in this treatment for schizophrenia. Continued observations and research are necessary to obtain final results and to interpret current results. Guidelines are offered based on existing and prospective progress—Journal abstract, modified.

4676. Oei, T.P.S., and Tan, E.S. (La Trobe University, Bundoora, Victoria, Australia) Companion program by university students and behavioral change in female chronic schizophrenics. Journal of Clinical Psychology, 37(1):96–100, 1981.

The effects of a companion program in effecting change in female chronic schizophrenic inpatients, and the effects of companion sex and the number of visits needed to produce change were investigated. Subjects included five female and four male third-year psychology student companions and two female and two male students who served as recorders. Thirty-six schizophrenics were visited by the students once, twice, or three times weekly for 7 weeks; a control group received no visits. The results show that only patient functional behavior in the three visits per week group showed significant improvement. This suggests that a minimum of three 30-minute visits per week is required to produce behavioral changes in chronic female schizophrenics. No effects of visitor sex on behavioral change of patients were found. (7 references)—Author abstract, modified.

4677. Pickar, D.; Davis, G.C.; Schulz, C.; Extein, I.; Wagner, R.; Naber, D.; Gold, P.; van Kammen, D.; Goodwin, F.; Wyatt, R.; Li, C.; and Bunney, W. (Biological Psychiatry Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20205) Behavioral and biological effects of acute beta-endorphin injection in schizophrenic and depressed patients. American Journal of Psychiatry, 138(2):160–166, 1981.

A dose of β-endorphin (4-15 mg)

was administered intravenously to six schizophrenic and four depressed patients in a double-blind study. No significant differences were found in behavioral ratings between these endogenous opioid peptides and placebo for the overall group or for either schizophrenic or depressed subgroups. Clinical worsening and improvement were observed in individual schizophrenic patients. There was no evidence of late appearing therapeutic effects in four schizophrenic patients rated for 5 consecutive days after placebo and drug infusions. In one patient, 10 mg of β-endorphin produced neuroendocrine effects comparable to those produced by 5 mg of intravenously administered methadone. In two other patients, it produced large increases in circulating opioid activity as determined by radioreceptor assay. These biological data support the notion that parenterally administered β-endorphin exerts significant opiatelike activity in vivo. (56 references)—Author abstract, modified.

4678. Pilsecker, C. (VA Medical Center, 5901 East 7th Street, Long Beach, CA 90822) Hospital classes educate schizophrenics about their illness. Hospital & Community Psychiatry, 32(1):60–61, 1981.

A lecture plus question and answer class, entitled "Let's talk about schizophrenia" has been developed for schizophrenic inpatients at the Long Beach Veterans Administration Medical Center. The class is held monthly and attendance is voluntary. The class consists of two 1-hour sessions aimed at educating patients about their illness—the meaning of schizophrenia, methods of diagnosis, theories of etiology, and some treatments. Over the first 6 months, 67 patients have attended one or both sessions. Most patients appeared attentive in class, and patients asked many questions. Of 32 patients who attended both classes, 77 percent reported finding the classes very useful, and 23 percent reported finding them somewhat useful. In addition 97 percent said they had learned something new. (1 reference)

4679. Schooler, N.R. (Psychopharmacology Research Branch, National Institute of Mental Health, Rockville, MD 20857) Placebo effect: From control to experimental condition. In: Baxter, C., ed. Perspectives in Schizophrenia Research. New York: Raven Press, 1980. pp. 389–399.

Methodological issues raised about the design of placebo studies are examined. Several examples are given to suggest that the administration of inert substances can provide information about the biological state of individuals being studied. It is suggested that the understanding of both the positive and negative effects of drugs used in the treatment of schizophrenia makes studies which use placebo treatments innovatively both clinically and ethically appropriate. The discussion that followed the presentation of the paper at a symposium on strategies for future research in schizophrenia is given. (24 references)

4680. Sevestre, P.; Coloni, F.; and Lagrange, J. (Hôpital Esquirol, Charenton—Saint-Maurice, France) Distinguishing schizophrenias by means of pharmacotherapy. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. B. Amsterdam: Elsevier/North Holland, 1979. pp. 1101–1104.

The factors that affect the decision to treat schizophrenics with long-acting antipsychotic medications are discussed. Therapeutic evidence indicates that: (1) different patients with identical symptomatology can present different tolerance to the same drug; (2) the same patients can demonstrate different clinical reactions to the same drug; and (3) a single patient can present different tolerance to the same drug. Hard evidence on the therapeutic efficacy of each antipsychotic medication is unavailable due to the varying reactions. It is concluded that the prescribing physician must handle each case individually.

4681. Thulesius, O., and Nielsen, F. (Department of Physiology, Centrallasarettet, S-35185, Vaxjo, Sweden) Drug induced arterial hypotension in psychiatric patients treated with dihydroergotamine. Nordisk Psykiatrisk Tidsskrift, 33(2):79–84, 1979.

Orthostatic hypotension with symptoms of decreased blood flow and mental retardation was examined among hospitalized psychiatric patients receiving major tranquilizers. Sixty-five patients with previously known orthostatic complaints such as dizziness and faintness on standing, dimming of vision, generalized weakness, and occasionally syncope were tested with a standard orthostatic test which included measurement of blood pressure, electrocardiogram, and heartrate after resting control periods. The majority of patients had chronic psychosis (schizophrenia, $n = 39$) and depressive psychosis ($n = 16$) with various other disorders in the remainder. All patients received neuroleptics and/or thymoleptics and other tranquilizers. After a washout period of 1 week of placebo (no blood pressure elevating drugs) and maintenance of psychotropic drugs, a new orthostatic test was performed. Thereafter certain patients were randomly given hydroergotamine (DHE) at an oral dosage of 5 mg two times per day. A repeated evaluation was performed after 1 week. Results are discussed in terms of the prevalence of orthostatic pathological reactions and orthostatic symptoms in 28 percent of the hospitalized patients. Treatment with appropriate doses of dihydroergotamine (2.5 mg times 4) decreased blood pressure fall and orthostatic symptoms. The most pronounced cases of orthostatic blood pressure fall were found among patients receiving a combination of psychotropic drugs and with extrapyramidal symptoms. (7 references)

4682. Trbovic, M. (Psihijatrijska klinika Medicinskog fakulteta Sveucilista, Zagreb, Yugoslavia) Problems of interpretation in the individual psychotherapy of schizophrenics. Socijalna Psihijatrija, 7(4):375–381, 1979.

Problems in interpreting the individual psychotherapy of schizophrenic patients are examined. Psychopathologic phenomena are viewed as directly experienced psychic processes with an essential and authentic determination of meaning in the patient's behavior and a manifestation of specific schizophrenic symptoms and mechanisms. The process of interpretation in the total therapeutic process depends on a series of elements which determine the interpersonal exchange between patient and therapist and on the character of the schizophrenic disorder and the interference of the environment. All of these elements should be considered and continuously studied in order to secure successful treatment. Interpretations that are not based on the patient's psychopathological specific content and mechanisms inevitably assume an arbitrary character and harm the therapeutic process. The therapist's personality and professional ethics are also important variables. (20 references)—Journal abstract, modified.

4683. Tune, L.E.; Creese, I.; DePaulo, J.R.; Slavney, P.R.; and Snyder, S.H. (Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205) Neuroleptic serum levels measured by radioreceptor assay and clinical response in schizophrenic patients. Journal of Nervous and Mental Disease, 169(1):60–63, 1981.

Serum neuroleptic levels and clinical response were compared serially in 10 schizophrenic patients treated with a variety of neuroleptics using a novel radioreceptor assay for neuroleptics. In this assay, the drug in serum competes with (^{3}H) spiroperidol for binding to dopamine receptors on membranes of the caudate nucleus. Serum neuroleptic levels, expressed in terms of dopamine receptor occupancy, were similar for most neuroleptics at therapeutic doses. Thioridazine levels were substantially higher than those of other neuroleptics. (24 references)—Author abstract.

4684. Vranckx, C.; Minne, P.; Benghezal, A.; Moeglen, J.M.; and Audibert, A. (Hôpital Psychiatrique, Tienen, Belgium) Vasopressin and schizophrenia. In: Obiols, J.; Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. A. Amsterdam: Elsevier/North Holland, 1979. pp. 753–758.

The effectiveness of lysin-8-vasopressin—administered after a washout period without placebo at a daily dose of 7.5 to 45 I.U. as a nasal spray—was assessed over a 4-week period in 16 chronic schizophrenic patients. Response was evaluated at 3, 7, 14, 21, and 28 days on the Brief Psychiatric Rating Scale, and a final overall assessment was made on day 28. The tolerance and safety parameters included an ECG and laboratory tests before and after treatment, along with measurements of pulse, blood pressure, and urinary output throughout the trial. Fourteen subjects improved on vasopressin, and in three the improvement was spectacular. Tolerance was excellent. Future research should evaluate these findings and study the relationship between vasopressin and the endorphins. (11 references)—Author abstract, modified.

4685. Wessels, W.H., and Gosling, J.A. (Department of Psychiatry, University of the Orange Free State, Bloemfontein, South Africa) The clinical efficacy of clozapine as compared to laboratory parameters. In: Obiols, J.;

Ballus, C.; Gonzalez Monclus, E.; and Pujol, J., eds. Biological Psychiatry Today. Vol. B. Amsterdam: Elsevier/North Holland, 1979. pp. 959–962.

Clozapine, a piperazine derivative of dibenzodiazepine, was administered to 15 hospitalized schizophrenics to ascertain its clinical efficacy, side effects, and effect on blood pressure and pulse rate, as well as to determine the serum levels of the drug itself and the drug plus its metabolites. The results indicate that: (1) clozapine is effective in treating schizophrenia; (2) the supine pulse rate offers a practical indication of expected serum levels of the drug plus its metabolites and is helpful in checking patient compliance; (3) serum levels reach steady-state on day 5 and maximum side effects occur on the same day; (4) serum levels cannot assist in determining therapeutic efficacy or side effects; (5) no accumulation occurs during the first 6 weeks; and (6) a certain period of exposure to a constant serum level is necessary for clinical improvement. (3 references)—Author abstract, modified.

VII World Congress of Psychiatry

The **VII World Congress of Psychiatry** will be held from **July 11 to July 16, 1983, in Vienna, Austria.** The scientific program will provide a review of developments in psychiatry over the last decade and a preview of the advances expected to occur over the coming one. Plenary session topics will include: Nomenclature and Classification; Biological Aspects of Psychiatric Disorders; Sociological Aspects of Psychiatry/Genetics; Concepts of Neurotic and Personality Disturbances; New Trends in Inpatient and Outpatient Care; National Schools and World Psychiatry; Evaluation of Treatment Programs.

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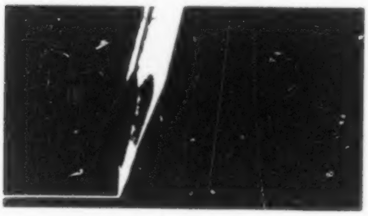

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